

SOME
ASYMMETRIC
ORGANOSILICON COMPOUNDS

A Thesis
presented for the degree of
Doctor of Philosophy in the Faculty of Science
of the
University of Leicester
by
Peter William Jones

The University, Leicester

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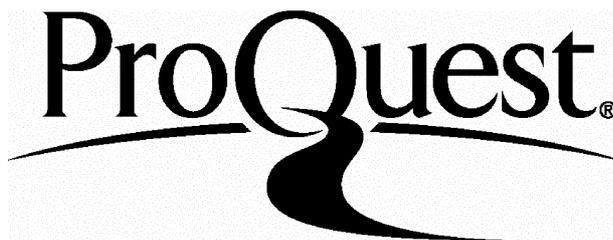
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STATEMENT

Except where otherwise stated, all the experimental work described herein was carried out by the author in the laboratories of the Department of Chemistry, University of Leicester between October 1959 and the present date.

The work has not been presented, and is not concurrently being presented, for any other degree.

October 1962

Signed: *P. W. Jones.*

I wish to thank my two supervisors, Dr. C. Eaborn (who suggested the topic) and Mr. R. W. Bott, for encouragement and help. I also thank Professor Hunter for his allowing my use of his laboratories.

Maintenance grants from, in turn, Imperial Chemical Industries (Nobel Division) and the Department of Scientific and Industrial Research are gratefully acknowledged.

Signed:

P. W. Jones

SUMMARY

A survey is made of the literature concerning the resolution of asymmetric organosilicon compounds and the application of stereochemical studies to the elucidation of the mechanism of nucleophilic substitution at silicon.

The preparation and resolution of p-[ethylmethyl(p-methoxyphenyl)silyl]benzoic acid (I) and its conversion into optically-active p-[ethylmethyl(p-methoxyphenyl)silyl]benzyl alcohol (II), p-[ethylmethyl(p-methoxyphenyl)silyl]benzyl methyl ether (III), and methyl p-[ethylmethyl(p-methoxyphenyl)silyl]benzoate (IV), is described. In all, eleven previously unreported compounds were isolated.

Unsuccessful attempts were made to prepare optically-active silicon-functional arylethylmethylsilyl- compounds by selective bromine cleavage of the p-methoxyphenyl - silicon bond of each of the compounds I, III, and IV, and subsequent treatment of the reaction mixture with isopropyl alcohol or lithium aluminium hydride. Explanations for the apparent lack of stereospecificity in these reactions are offered.

Optically-active methylphenyl(α-naphthyl)methoxysilane (V) was prepared, labelled with tritium in the methoxy group. The methanolysis of V in neutral, basic, and acidic, methanol was investigated: the pseudo first-order rate constant was determined for each reaction mixture, both polarimetrically and [by Dr. R.

Baker and Mr. R. Spillett] radiochemically. For each reaction mixture, these two values of the rate constant were identical within experimental uncertainty (<5 %). The significance of this result is discussed, and an analysis is presented of the stereochemical requirements of those mechanisms of nucleophilic substitution at silicon which are currently postulated.

An attempt is made to rationalise, in terms of reaction mechanism, those stereochemical results of nucleophilic substitution at silicon as are available in the literature.

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INTRODUCTION

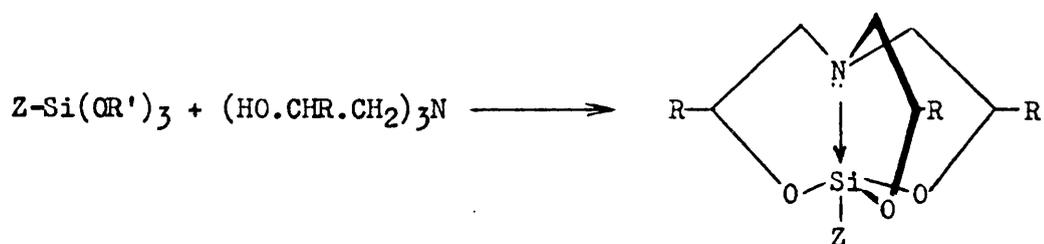
PART ONE: The Resolution of Optically-Active Organosilicon Compounds.

(A) General

Since silicon is placed in the same group of the Periodic Classification of the elements as carbon, having a similar electronic configuration in the ground state, viz ns^2np^2 (carbon, $n = 2$; silicon, $n = 3$), formal similarity of stereochemistry is to be expected.²³ In fact, silicon(IV) has tetrahedral disposition of bonds in those compounds examined by X-ray techniques, and hence presumably has sp^3 hybridisation, as has carbon. Nevertheless, the silicon atom differs from the carbon atom in having available readily accessible 3d orbitals. The effect of the presence of these 3d orbitals is sometimes difficult to predict, but they are responsible for the differences between the mechanisms of nucleophilic substitution at silicon(IV) and carbon.

Silicon is able to form stable compounds in which the coordination number is 5 or 6. The usual example of this property is the fluorosilicate ion, SiF_6^{2-} , which has been shown by X-ray crystallography to have an octahedral structure, and hence sp^3d^2 hybridisation of bonds. The ion $[Si(acetylaceton)_3]^+$ has been resolved²⁷ into its optical enantiomers, showing again the octahedral configuration and therefore the participation of the 3d orbitals. A recent⁵ example of silicon's forming pentacoordinate complexes is that of Frye, et al.: the condensation of trialkoxysilanes with triethanolamines lead to the exclusive formation of crystalline monomeric

products which were formulated as follows:



where R = H, Me; Z = H, Me, Octadecyl, α -Phenethyl, Vinyl, Phenyl, Ethoxy, and (-)-Menthoxy.

The products were designated as triptych siloxazolidines, and the silicon atom was believed to be pentacoordinate as a result of transannular dative bonding between nitrogen and silicon. The authors considered that the hybridisation of the silicon atom was probably sp^3d , with the oxygen atoms coplanar with the silicon atom, and situated at the equatorial positions ($\widehat{\text{OSiO}} = 120^\circ$) while the nitrogen atom and Z (the remaining substituent) occupied the axial positions.

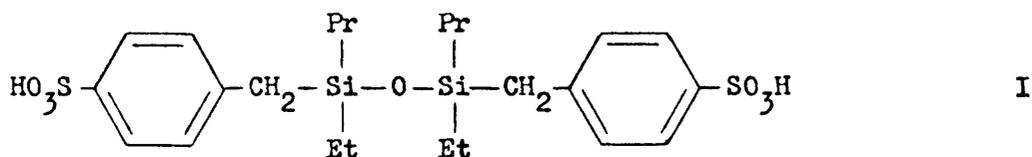
Initially,¹ interest in the stereochemistry of silicon(IV) was limited to trying to show that asymmetric organosilicon compounds* were capable of resolution into optical enantiomers in the manner of carbon compounds. At this time, the significance of stereo-

* This expression will be used throughout this thesis to indicate asymmetry of the molecule about the silicon atom ONLY.

chemistry as it affected the mechanism of substitution at carbon was scarcely realised, if at all. Accordingly, organosilicon compounds prepared and resolved with the above problem in mind contained no silicon-functional groups, these being too labile for convenience. On the other hand, those organosilicon compounds prepared and resolved for the purpose of investigating the stereochemistry of substitution at silicon have naturally been silicon-functional.

(B) Carbon-functional optically-active organosilicon compounds.

The first example of an optically-active organosilicon compound was reported in 1907, by Kipping, who resolved diethyldi-n-propyldi-p-sulphobenzylidisiloxane (I) by means of its methylhydrindamine salt.^{1,2}



Apart from the ambiguity of two asymmetric centres per molecule, i.e., the possibility of dealing with the meso-form, the work had some unsatisfactory features:

- (i) The free acid was not isolated, although the sodium salt was obtained as a solid.²
- (ii) The sparingly-soluble salt (α), obtained from repeated crystallisations of the d-methylhydrindamine salt of the (+)-

acid (I), had practically the same specific rotation as the optically-impure more-soluble diastereoisomer (β) recovered from the mother liquors. However, the melting points of α and β were quite different, being 205° and 133° respectively.

(iii) Decomposition of the salt α by means of sodium carbonate and subsequent boiling off of the d-methylhydrindamine gave a feebly optically-active solution having the same sign of rotation as the resolving agent. The use of l-methylhydrindamine as the resolving agent gave eventually the laevorotary sodium salt. It could therefore be argued that the observed rotations were due entirely to residual amine.

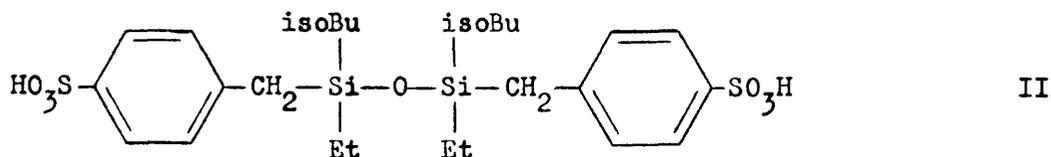
Kipping showed the enantiomorphous relationship of the (+)- and (-)-sodium salts of I thus obtained (using d- and l-methylhydrindamine respectively), by converting either one into first the d-methylhydrindamine salt, then into the l-methylhydrindamine salt. The two resultant salts being quite different in melting point (but not in specific rotation), they must have been diastereoisomeric, and hence the parent sodium salt an optical enantiomer.

Further, the decomposition of the optically-impure diastereoisomer β (see (ii), above), by boiling it with sodium carbonate solution, gave a very faintly optically-active sodium salt solution, having the opposite sign of rotation to the resolving agent.

(iv) 1-Menthylamine salts of the separate (+)- and (-)- enantiomers of the acid (I), showed no difference in specific rotation. The melting points, also, of these diastereoisomers showed no difference. In fact, only the resolving agent that worked (i.e., d- and l-methylhydrindamine) showed the expected differences of melting point between diastereoisomers, and even in that case the specific rotations were identical. Chinchonidine and d-bornylamine resembled l-menthylamine in this respect.

Kipping concluded that "in spite of the curious combination of indications to the contrary", the racemic acid (I) had been resolved.

Di-iso-butyldiethyldi-p-sulphobenzylidisiloxane(II) was later reported³ to have been resolved similarly.



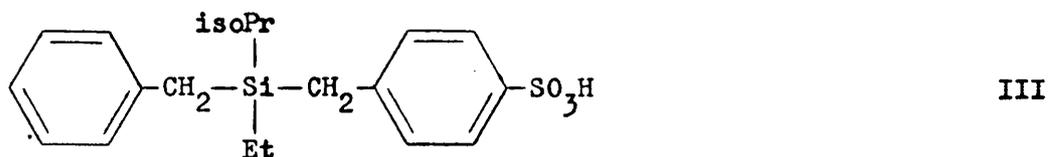
Although the specific rotations of the isolated optically-pure sodium salts were twice as large as for the enantiomers of the related acid (I), the sign of rotation was still the same as that of the methylhydrindamine employed in the resolution. However, the optically-impure more-soluble diastereoisomer gave a sodium salt having a more definitely opposite rotation than was obtained (in (iii), above), for compound I. E.g.,

pure l-methylhydrindamine salt $\xrightarrow{\text{boiled with Na}_2\text{CO}_3 \text{ soln.}}$
 Na salt soln., $[\alpha]_D = -10.5^\circ$

oily, impure " " $\xrightarrow{\text{boiled with Na}_2\text{CO}_3 \text{ soln.}}$
 Na salt soln. $\alpha = \sim +0.5^\circ$

By contrast with the acid (I), the l-menthylamine salts of the (+)-, (-)-, and (\pm)- acid (II) showed a difference in melting points and also in specific rotations. However, the d-bornylamine salts displayed no such differences.

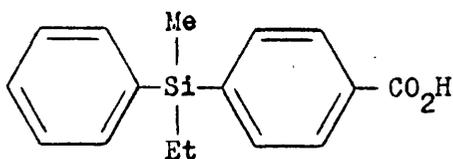
For the same reasons, the resolution of benzylethylisopropyl-p-sulphobenzylsilane(III) was also difficult to demonstrate.⁴



The brucine salt of the acid (III) was separable into a less-soluble component, m.p.205°, and a more-soluble component, m.p.120-130°, but the specific rotations of these two (presumed) diastereoisomers were again identical. Solutions of the respective sodium salts of III obtained from these two brucine salts were of opposite sign, having $[\alpha]_D \pm \sim 1^\circ$. Although five pairs of salts [(+)- acid + l-base), and (\pm)- acid + l-base)] were examined (base = menthylamine, strychnine, cichonidine, quinine, and morphine), "in no case was there a difference in melting point or specific rotation well

outside the limit of possible experimental error".

Because of the anomalous properties of the diastereoisomeric salts of the three acids I, II, and III, the much more recent resolution²⁸ of *p*-(ethylmethylphenylsilyl) benzoic acid (IV) is of importance as representing the first indisputable example of an optically-active asymmetric organosilicon compound.



IV

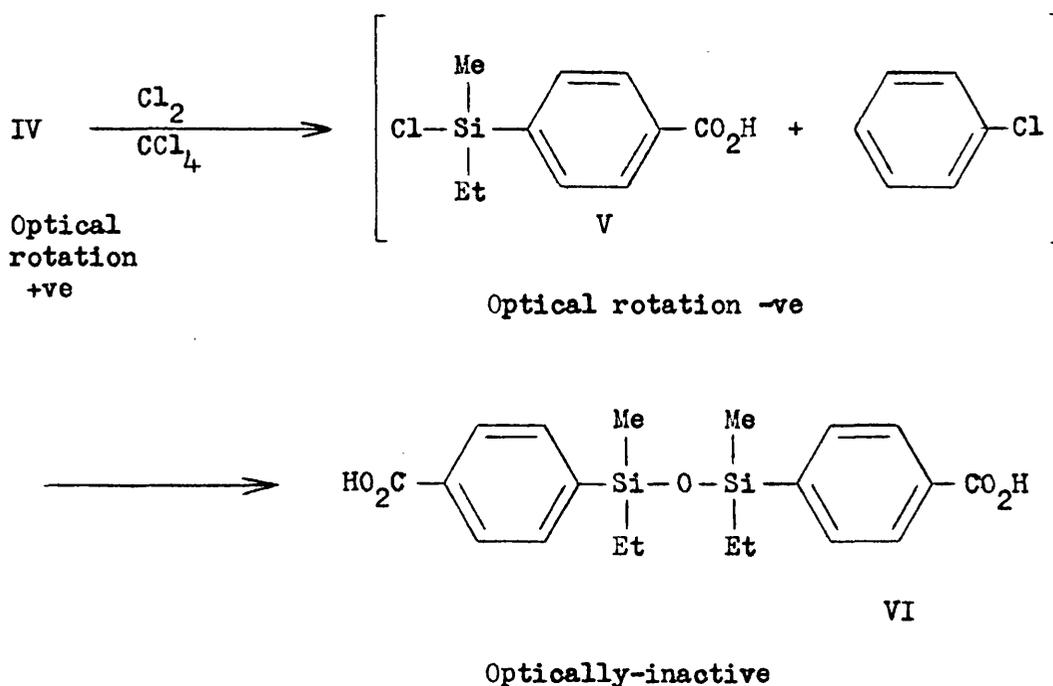
Compound IV was isolated as a crystalline solid, and resolved by successive crystallisations of its (-)-quinine salt to constant melting point. Regeneration of the acid from the less-soluble diastereoisomer gave an enantiomer of unchanged melting point, and of specific rotation $+ 2.8^\circ$, i.e., of opposite sign to the resolving agent. It is noteworthy, however, that the various fractions of recrystallised diastereoisomers, containing varying amounts, therefore, of (+)(-)- and (-)(-)-salts had identical specific rotations, confirming Kipping's observations.

Further, it was possible to subject the optically-active acid IV to several reagents to ascertain the optical lability of Si - C bonds:- E.g., the substituted benzoic acid IV did not racemise when kept molten at 100° for 6 hours. Similarly, alcoholic

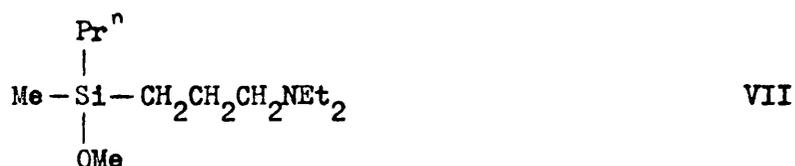
and aqueous-alcoholic alkali, and glacial acetic acid, had no effect on the optical activity. Kipping had noticed some reduction in optical activity on heating his enantiomeric acids (I, II, III) with caustic alkali, or sodium carbonate, but concluded⁴ that this was the result of cleavage of the Si - benzyl bond. He was unable, therefore, to be certain that Si - C bonds are optically stable.

(C) Silicon-functional optically-active organosilicon compounds.

Although Pitt²⁹ probably produced p-(ethylmethylchlorosilyl)-benzoic acid (V) in an optically-active solution obtained from the chlorination of the corresponding acid (IV), he was unable to isolate any optically-active material, obtaining only optically-inactive disiloxane (VI) on working up the mixture:



Kirschner has resolved N,N-diethyl- γ -(methoxymethylpropylsilyl)propylamine (VII), by means of its dibenzoyl d-hydrogen tartrate.

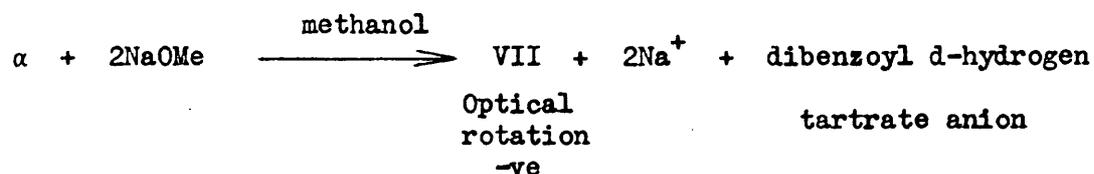


However, like Kipping (section B), he was unable to isolate the optically-active organosilicon base VII from the corresponding diastereoisomeric salt (α). Aqueous alkali could not be used to displace the resolving agent, so N-ethylpiperidine was used instead. Trial experiments with the dibenzoyl d-hydrogen tartrate of triethylamine showed that N-ethylpiperidine displaced the weaker base, and that filtration of the resulting mixture removed all the resolving agent (as the N-ethylpiperidine salt). The diastereoisomer α (see above) on treatment with N-ethylpiperidine, followed by filtration, gave an N-ethylpiperidine solution having laevorotatory properties [the resolving agent is also laevorotatory] which rapidly diminished (i.e., racemisation occurred) - the compound having a half-life of approximately 1.5 minutes. Extrapolation of the observed rotations gave $[\alpha]_D = -30.1^\circ$ at zero time, i.e., for the optically pure enantiomer of the base VII.

The more-soluble diastereoisomer (β) was obtained only as

an impure syrup. Cleavage, etc., in N-ethylpiperidine solution, as above, gave a filtrate (3 minutes after the addition of the N-ethylpiperidine) having a rotation of + 0.019°.

Kirschner was also able to study the optical stability of the organosilicon base (VII) towards methanol and methoxide ion: the addition of two equivalents of methoxide ion (in methanol as solvent) to the diastereoisomeric salt α (see above) gave the free base (VII) in methanolic solution.



The dibenzoyl-d-hydrogen tartrate anion was present throughout, so a blank was run, using triethylamine instead of the organosilicon base (VII). Sodium dibenzoyl-d-hydrogen tartrate (presumably) was slowly precipitated during the reactions, thereby reducing the observed rotation in each system. The difference between observed rotations of the two systems at any one time was taken to be the rotation due to the optically-active enantiomer of the base (VII). This difference (i.e., the optical activity of the base (VII)) remained approximately constant for the first 25 hours, then decreased slowly after that time.

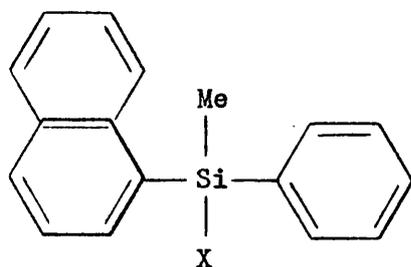
If, after 12 hours, a further two equivalents of methoxide

ion were added, the observed rotation began to decrease after one hour.

Hence, the organosilicon base (VII) was found to be readily racemised by N-ethylpiperidine (and also by piperidine), but to be virtually stable towards neutral methanol, and to be only slowly racemised by methoxide ion.

Because of these properties of the base (VII) [quite apart from the unsatisfactory regeneration of the enantiomers, especially when the optically-pure enantiomer had the same sign of rotation as had the resolving agent], Frye²⁰ has cast some doubt on the authenticity of the above reported resolution. Unsuccessful attempts in this Laboratory to repeat this work have also indicated that Kirschner was in error³⁷.

Sommer and Frye have prepared optically-active organosilicon compounds of the general formula, (VIII):^{12,13,14,15,20,30}



X = H, Cl, F, OH, OMe
(inter alia)

VIII

isolating each compound (except the silanol, VIII; X = OH) as a crystalline solid. Resolution was effected by means of the l-menthoxide (VIII; X = l-menthoxy-), both diastereoisomers being obtained crystalline, although one was not optically-pure.

Reduction, by means of lithium aluminium hydride, of the diastereoisomers gave the two optical enantiomers of the silane (VIII; X = H), which was the starting point for all subsequent preparations. E.g., chlorination of the optically-active silane (VIII; X = H) gave the optically-active chlorosilane (VIII; X = Cl), and treatment of the latter with methanol in the presence of a hydrogen chloride acceptor yielded the optically-active methoxide (VIII; X = OMe).

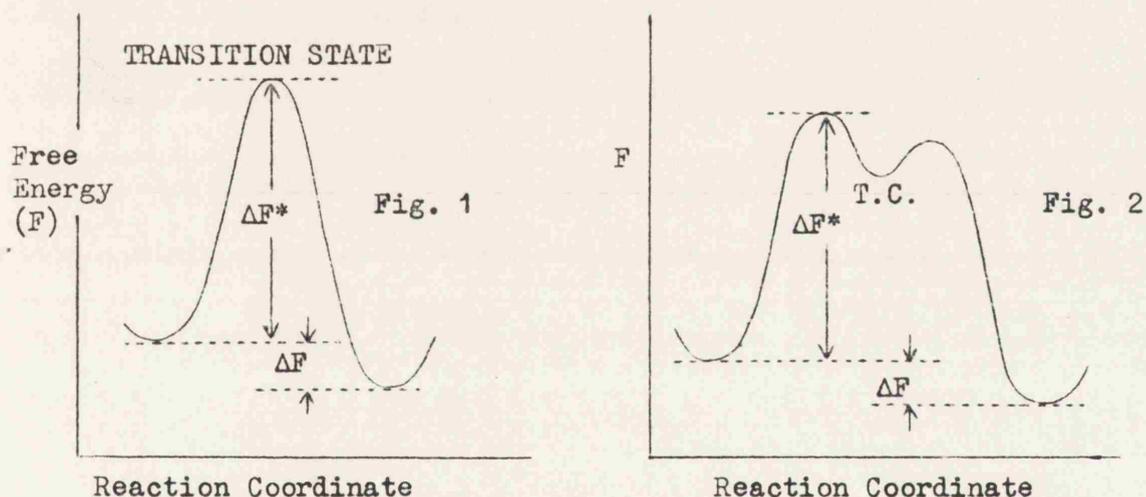
By contrast with Kirschner's compound (VII), the optically-active methoxide (VIII; X = OMe) was said to be optically stable in piperidine, and in triethylamine, solution, but to be rapidly racemised in methanol solution²⁰.

More important, by a series of interconversions (see below) involving the methylphenyl(1-naphthyl)silyl- derivatives (VIII), Sommer and Frye were able to show the predominant stereochemical path of many substitutions at silicon, and hence were able to speculate on the mechanism of substitution at silicon to greater effect than was formerly possible.^{12,13,14,15,20,30}

PART TWO: The Stereochemical Approach to the Mechanism of Nucleophilic Substitution at Silicon.

A reaction mechanism may be defined as a structural description of each transition state and each intermediate involved in the reaction sequence (ref. 11, p.638). The many studies made of the mechanism of nucleophilic substitution at carbon have employed both stereochemical and kinetic observations as criteria. Tran-

sition state theory requires that any such reaction proceeds via a hypothetical "transition state", made up of one or more reactant molecules, the energy for the formation of which is represented by the "free energy of activation" of the reaction. This energy-barrier to the formation of the transition state thus determines its rate of formation, and hence the rate of the overall reaction. The free-energy profile of the reaction may be represented as in Figure 1



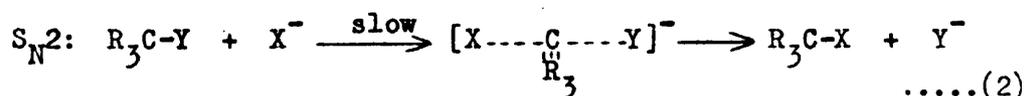
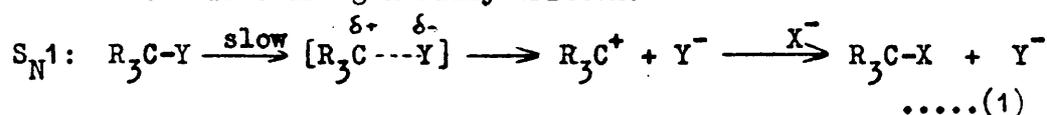
where ΔF^* is the free energy of activation, and ΔF is the free-energy of reaction. The zero point energies of reactants and products have been ignored.

For a reaction sequence involving two or more transition states, the rate is determined by the transition state of highest energy. The reaction profile might then be as in Figure 2.

In the case of nucleophilic substitution at saturated carbon, two limiting mechanisms³⁸ are recognised, designated as⁴² S_N1 and S_N2 , i.e., nucleophilic substitution in which the rate

determining step (the formation of the transition state) involves ONE and TWO molecules respectively, ignoring solvation effects.

These mechanisms are generally written:



Solvation, although very important, has been omitted from these schemes for clarity; in fact electrostatic solvation and desolvation of ions in polar solvents can have an energetic importance comparable to that of the formation and fission of covalent bonds.⁴³

Stereochemically, the two mechanisms have differing requirements. The S_N1 mechanism, as described above, gives rise to a "free" (actually solvated) carbonium ion having sp^2 hybridisation of bonds, and therefore of flat configuration. The products of such a reaction involving the "asymmetric atom" of an optically-active substrate should, therefore, be racemised. However, under certain conditions, predominant retention or inversion of configuration occurs, and it is then assumed that the intermediate carbonium ion is unable to become planar before reaction with a nucleophile, either because of electrostatic configuration-retaining forces within the ion (see discussion of the Walden Inversion, below), or because of "shielding" of one side of the carbonium ion by the leaving group.³⁴

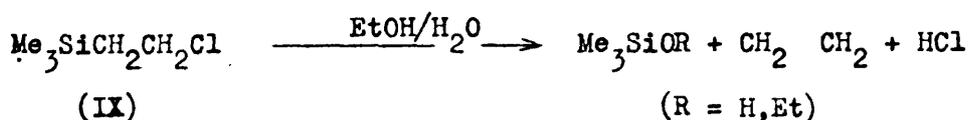
The S_N2 mechanism requires stereochemical inversion of

configuration always, because carbon is incapable of a valency greater than four. The three "inert" bonds to R_3 (equation 2, above) change from sp^3 to (approximately) sp^2 hybridisation in the transition state, while the two "semi-bonds" of the transition state are obtained by overlap of the bonding orbitals of the entering and leaving groups (X and Y respectively) with the one remaining p orbital of the central carbon atom. Therefore, the angle between X and Y, relative to the central carbon atom, must be 180° . As a consequence, the stereochemical course of a replacement reaction at carbon can be used as a criterion of mechanism.

Because of the relative accessibility of the 3d orbitals, it has often been postulated^{6,17} that substitution at silicon may occur via a third mechanism (as opposed to S_N1 -like and S_N2 -like mechanisms), in which a penta- (or hexa-) covalent silicon complex is formed as an intermediate. The free energy profile would then be as shown in Figure 2 (p.13), where the silicon complex is represented by "T.C.". This complex is supposed, in principle, to have a real existence (i.e., to be detectable by physical means). The transition states lying on either side of the complex are supposed to resemble the complex, i.e., the bonding in the transition states has some "d-character" (see below, p.20). These transition states are thought to be correspondingly stabilised (i.e., at a lower energy) as compared with the single transition state of an S_N2 -like reaction that does not employ d orbitals (Figure 1, p.13). Therefore, bimolecular reaction is thought to be

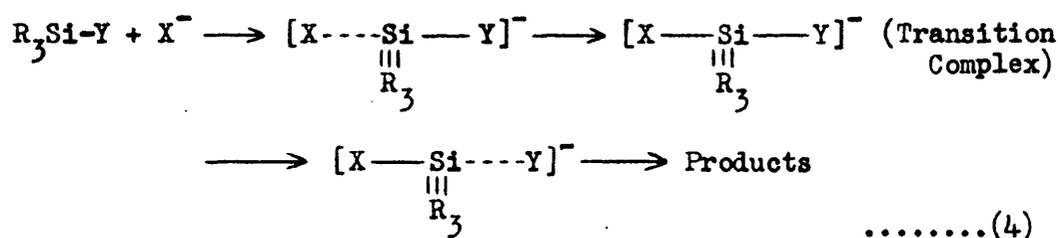
facilitated by the presence of the d orbitals of silicon, and this is the main reason advanced to explain the extreme rarity of siliconium ion intermediates (i.e., of the S_N1 -like mechanism); only very recently has evidence for the existence of siliconium ion intermediates been obtained:-

Sommer and Baughman⁴⁴ showed that β -chloroethyltrimethylsilane (IX) resembled t-butyl chloride in its solvolysis reactions in that its solvolysis rate (in aqueous ethanol), although insensitive to the nucleophilic character of the solvent, was strongly dependent on its ionising power (i.e., on the proportion of ethanol):



In addition, the solvolysis rate constants of the organosilicon compound (IX) and t-butyl chloride were approximately equal in corresponding media, and therefore it was argued that the transition states of the two solvolysis reactions were similar. In agreement, electron-withdrawing substituents (e.g., C_6H_5^- and $\text{m-CF}_3\text{-C}_6\text{H}_4^-$) on the silicon were found to retard the solvolysis rate.

Further, the rate of solvolysis of IX in 50% ethanol was found to be scarcely affected by the addition of potassium hydroxide to make the solution 0.54 M in alkali, but the rate in 70% ethanol was increased, on adding the same amount of alkali, by a factor of 4.2, although the rate was still lower than that



Equation 3 is analogous to Equation 2 (p.14) representing the S_N2 mechanism of carbon, and its stereochemical requirements are the same. The carbon analogue of Equation 4 has been suggested by Gillespie.¹⁰ Such a mechanism allows for X to be at angles other than 180° to the Si - Y bond, and therefore retention of configuration is possible.

Very recently, kinetic evidence for the formation of a transition complex has been claimed³⁰ for a substitution reaction at silicon, but no details are yet available. However, kinetic results are generally unhelpful in distinguishing the two possible bimolecular mechanisms, since the rate of a reaction is dependent only on the transition state of highest energy and not on the transition complexes (if any). Nevertheless, some important conclusions may be derived from consideration of "symmetrical" displacements (where X and Y are chemically identical) at silicon, and these studies are dealt with below (p.25).

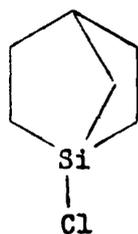
Stereochemical studies therefore have been much used in attempting to show the existence of a mechanism involving transition complex formation. These studies follow three distinct but overlapping lines, which have also been employed in investigating the stereochemistry of substitution at carbon:-

- (1) Studies concerning reactivity at a bridgehead.
- (2) Studies concerning symmetrical "Walden Inversions", using isotopic-labelling for following the reaction.
- (3) Studies concerning overt "Walden Inversions", requiring optically-active substrates.

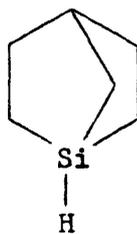
These methods will now be discussed in more detail:-

(1) Stereochemical Evidence Derived from Investigation of Substitution Reactions at Silicon Which is Situated at a Bridgehead or in a Related Monocyclic Compound.

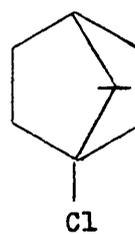
The bridgehead compound 1-chlorosilabicyclo [2.2.1]-heptane (X) was reported by Sommer and Bennett⁶ to have properties typical of an acyclic chlorosilane: it had an acrid odour, it was hydrolysed rapidly in a stream of moist air, and it underwent rapid quantitative titration of the Si - Cl bond with N/10 alkali. Also, it reacted rapidly with lithium aluminium hydride, in ether, to give the parent silane (XI).



X



XI



XII

Bartlett and Knox¹⁸ had earlier prepared 1-chloroapocamphane (XII), and shown it to be quite inert, e.g., refluxing with ethanolic silver nitrate solution gave no reaction after 48 hours. The

deduction was that bimolecular substitution at carbon requires "rear" attack by a nucleophile, and that no other geometry of transition state is possible. (This conclusion had been deduced earlier from other work, see below, p.25.)

Sommer and Bennett claimed that the reported facts concerning the reactivity of the bridgehead chlorosilane (X) accorded with a "preliminary working hypothesis" comprised of the following three postulates:

- (a) Nucleophilic displacements at silicon may involve the formation of an addition complex with the attacking reagent.
- (b) The geometry of the complex approximates to that of a trigonal bipyramid, and the bonding is sp^3d .
- (c) Entering and leaving groups need not be at an angle of 180° as for substitution at saturated carbon. Instead, the entering and leaving groups may be at an angle of approximately 90° to each other (i.e., "flank attack").

As Sommer and Bennett pointed out, postulate (a) had been proposed as early as 1927, but postulate (c) they claimed to be completely new for silicon. In fact, Gillespie¹⁰ had made similar observations on the stereochemistry of substitution at saturated carbon, when considering the effects of participation of the $3d$ orbitals (see above, p.18).

Sommer and Bennett's hypothesis can be represented as in Figure 3 (omitting the transition states):

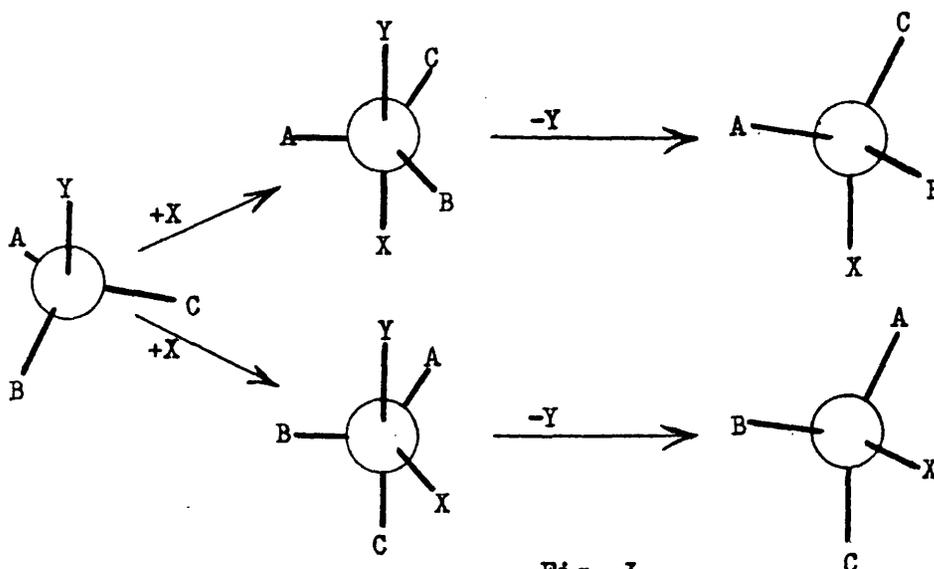
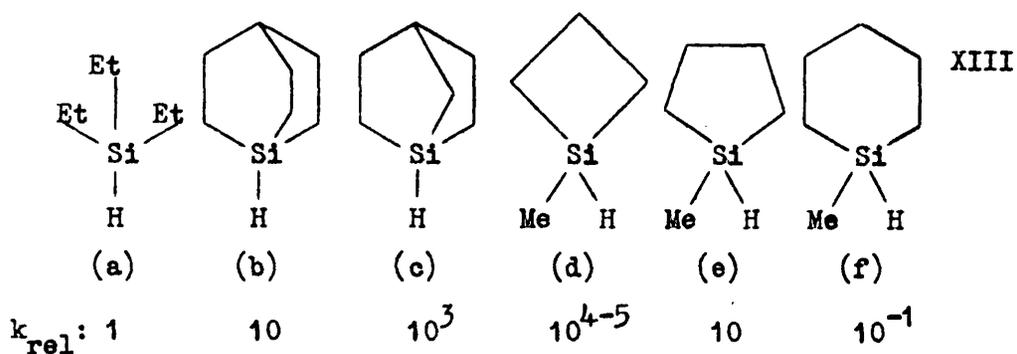
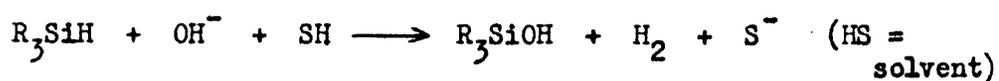


Fig. 3

Sommer, et al., have adduced further evidence for their hypothesis from a study of a series of cyclic and bridgehead^{7,8} silanes (XIII, (b)-(f)):



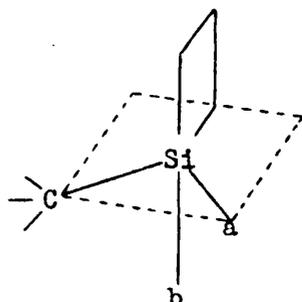
The second-order rate constants (k_2) for the reaction



were measured for the silanes shown above (XIII, (a)-(f)):

$$-\frac{d[\text{silane}]}{dt} = k_2[\text{silane}][\text{OH}^-]$$

The relative values of k_2 are given beneath the formulae. The authors pointed out⁷ that these results showed a complete reversal of the structure-reactivity relationships observed for displacements at carbon when the same comparisons are made, and they claimed that the facts accorded with the postulates outlined above (p.20), when the relative geometries of the ground and transition states are considered: all the compounds XIII, (b)-(f), have to react via the flank-attack mechanism, e.g., in the reaction of the silane XIII(d) with hydroxyl ion, the transition complex would be ideally as shown (XIV):



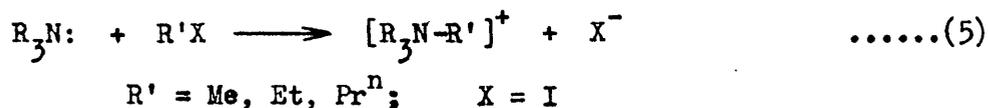
(i) a = H, b = OH

(ii) a = OH, b = H

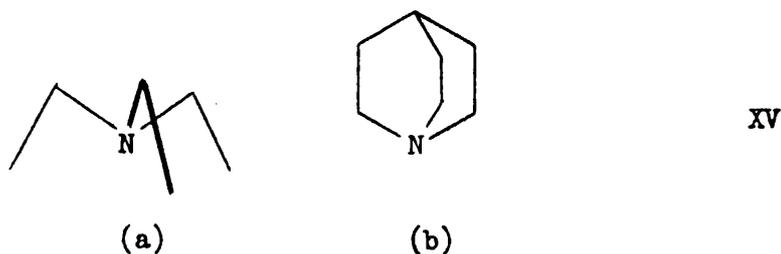
XIV

The structure-reactivity relationships of these silanes (XIII) were explained by reference to three factors:-

(1) Reduced steric hindrance to formation of a pentacovalent-silicon complex, due to groups on silicon being "pulled-back" in the ground state from the path of reagent attack. This may be compared with the investigations of Brown and Eldred³¹ on the relative rates of the Menschutkin reaction (Equation 5), employing triethylamine (XVa), and quinuclidine (XVb):



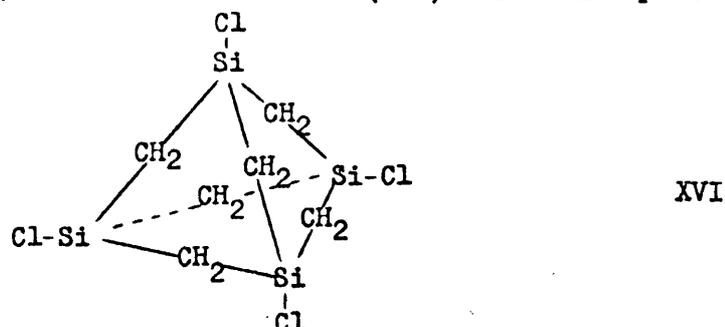
Although their basic strengths (*i.e.*, pK_b) are similar, it was found that triethylamine (XVa) reacted much more slowly than



quinuclidine (XVb) under comparable conditions, the effect becoming more pronounced as the size of the alkyl group R' of the alkyl halide increased.

- (2) The internal strain ("I-strain")¹⁹ in the pentavalent-silicon complex relative to the ground state.
- (3) The steric strain in the pentavalent-silicon complex relative to the ground state, due to increased crowding of groups in the former.

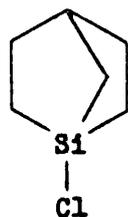
More recently, the bridgehead compound 1,3,5,7-tetrachloro-1,3,5,7-tetrasiladamantane (XVI) has been reported.⁹



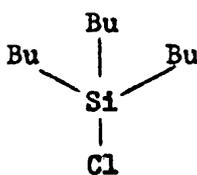
Unlike the bridgehead chlorosilane (X) (p.19), compound XVI was found to have practically inert Si - Cl bonds, being capable of dissolution in wet ether, followed by evaporation of solvent,

without suffering appreciable hydrolysis. This apparently anomalous lack of reactivity was explained by Sommer³² in a manner analogous to that adopted to explain the structure-reactivity relationships of the cyclic silanes XIII (p.21). He pointed out that compound XVI is practically strain-free in the ground state, unlike the bridgehead compound X. Rear attack by a nucleophile (e.g., OH⁻) is impossible with both compounds for steric reasons, while flank attack is less favoured on compound XVI because of the greater distortion of bond angles required to produce the necessary sp³d hybridised transition complex.

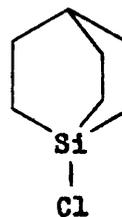
Further evidence cited by Sommer^{22,32} was the fact that of the following chlorosilanes (X, XVII, XVIII):



X

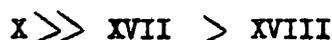


XVII



XVIII

the rates of reaction with lithium aluminium hydride were in the order:-

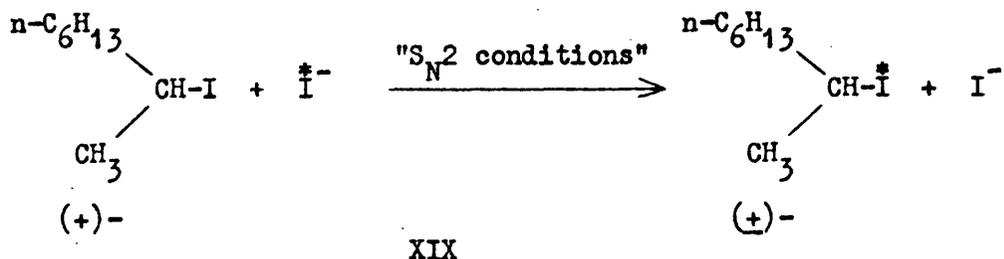


He suggested that tri-n-butylchlorosilane (XVII) reacts with lithium aluminium hydride in the "preferred" manner for chlorosilanes (i.e., by "rear attack", see p.32), while 1-chlorosilabicyclo [2.2.2.] octane (XVIII), a relatively unstrained bridge-

head chlorosilane, reacts more slowly than XVII because only the less-favourable mode of attack (i.e., "flank attack") is available. The high reactivity of 1-chlorosilabicyclo [2.2.1.]heptane (X), Sommer thought to be the result of the reduction of strain in the molecule in passing from the ground state to the transition complex, and hence to the rate-determining transition state; i.e., a form of steric acceleration³³ was proposed.

(2) Stereochemical Evidence Derived from the Kinetics of Symmetrical Substitution Reactions at Silicon, preferably Involving Optically-Active Substrates.

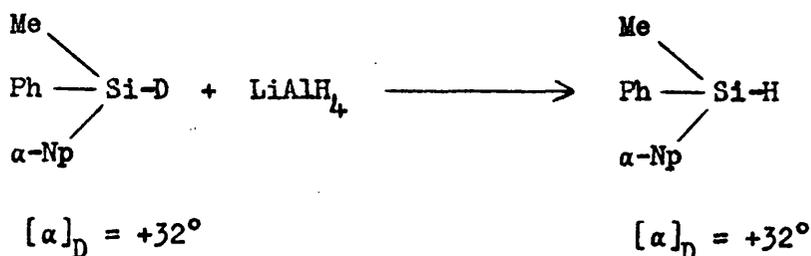
For carbon, such studies have been of great importance, e.g., the exchange of radio-active iodide ion with *s*-octyl iodide (XIX) showed the rate of inversion to be the same as the overall rate of exchange:³⁴



Other, similar, experiments gave the same result, i.e., each act of substitution at carbon produced inversion of configuration, under "S_N2 conditions".

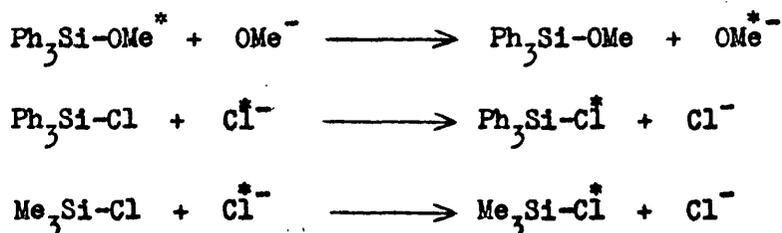
Ideally, the use of an optically-active substrate can afford evidence as to the relative ease of "rear" and "flank"

attack of a given nucleophile at silicon, but no kinetic studies have been reported although the exchange of protium for deuterium in an optically-active silicon compound has been followed qualitatively by the infra-red spectrum:¹²



It followed from the identical specific rotations of reactant and product that the reaction was highly stereospecific, and proceeded with retention of configuration.

The kinetics of the following reactions have also been examined:^{38,39,40}



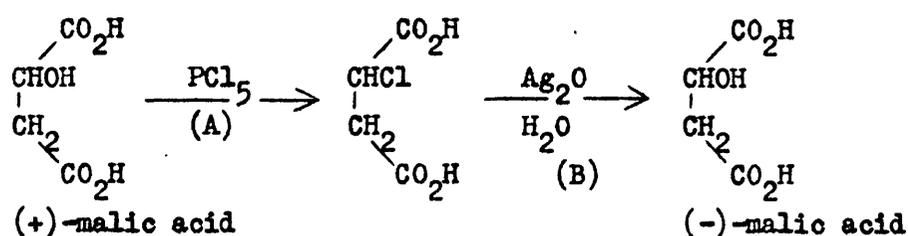
In each case the rate was quite low. Taking the first reaction as an example, the low rate of substitution means a high activation energy which in turn implies that the energy barrier to formation of the transition complex (if any) is appreciable, since for these symmetrical displacements, formation of a transition complex essentially constitutes reaction.

(3) Stereochemical Evidence Derived from "Walden Inversions" Involv-

ing Optically-Active Organosilicon Compounds.

The first Walden Cycles to be observed³⁵ involved malic acid,

e.g.,

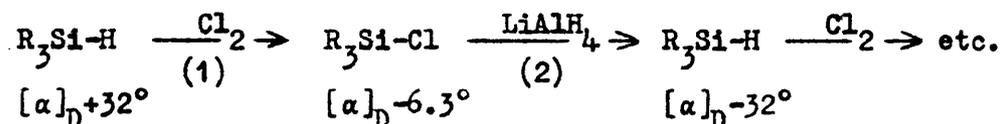


Evidently, of the reactions A and B in the above "equation", one (only) took place with inversion of configuration, while the other reaction occurred with retention, and both reactions were highly stereospecific. Nevertheless, on the above evidence it was not possible to state which of steps A and B gave inversion. [In fact, step A was invertive, while step B was retentive, the latter being due to the intermediate carbonium ion retaining its configuration³⁴ because of electrostatic forces between >C^+ and >CO-O^- .]

The fact that there is no necessary connection between configuration and sign of optical rotation of different asymmetric compounds, constitutes the main drawback to this approach to the elucidation of the stereochemistry of substitution. The problem was largely solved by Kenyon and Phillips,³⁶ who showed how to devise a Walden Cycle such that in the conversion of an optically-active compound to its enantiomer, only one step involves the "asymmetric atom", and therefore is the only step at which inversion of configuration can have occurred. However,

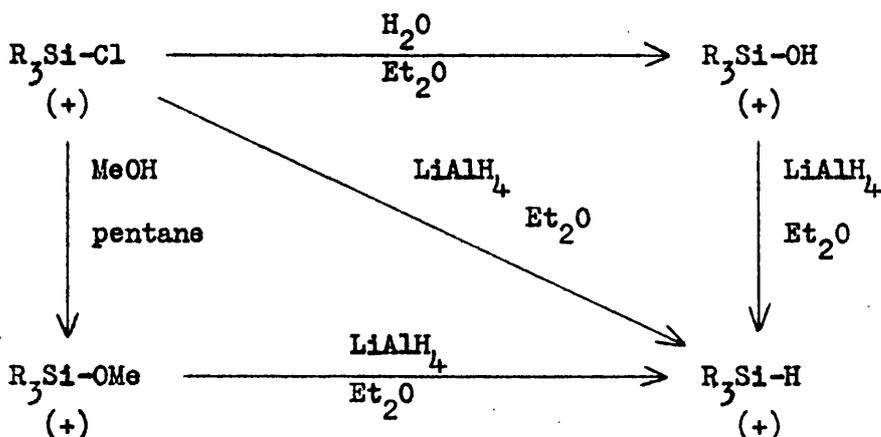
this scheme requires the functional group of the "initial" and "final" enantiomers of a Walden "Half-cycle" to be comprised of at least two atoms, e.g., -OH, but not -Cl.

The first Walden Cycle for organosilicon compounds was reported¹² by Sommer and Frye: ($R_3Si \equiv Me.Ph.\alpha-NpSi$)



In view of the ready reactivity of lithium aluminium hydride with bridgehead chlorosilanes (see p.19), Sommer and Frye tentatively chose step 2 as occurring by a retentive mechanism, but later on different grounds decided otherwise (p.31).

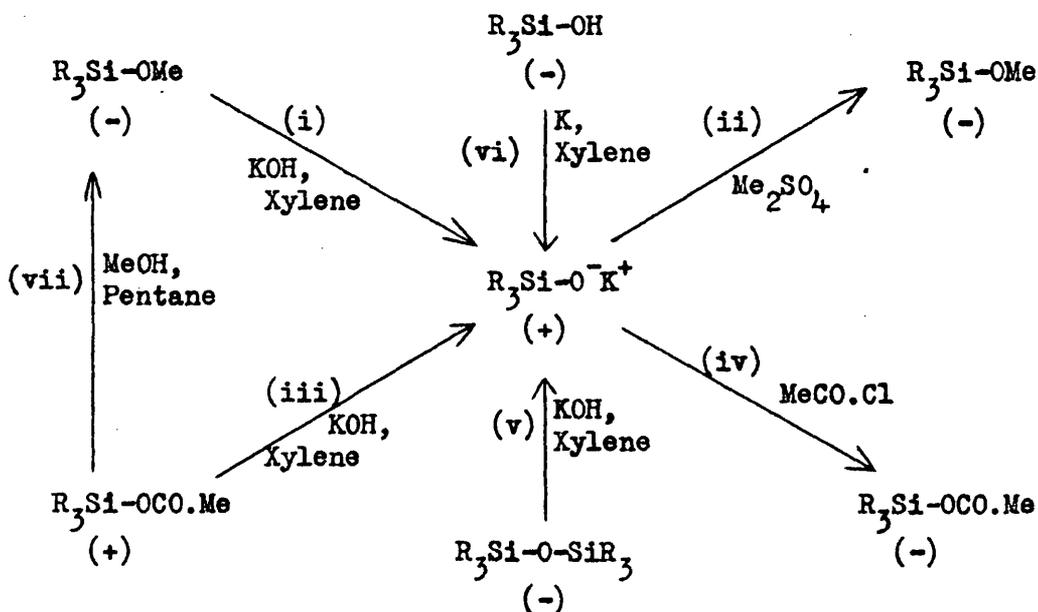
Other such interconversions by these authors were the following¹⁴ ($R_3Si \equiv$ as above):



As for reduction, hydrolysis and methanolysis of the chlorosilane were shown to be highly stereospecific, and the authors took this as evidence that planar siliconium ions could be ruled

out as intermediates in these reactions, in the particular solvents used.

In order to obtain chemical correlations of configuration and sign of optical rotation, Sommer and Frye made use of the method of Kenyon and Phillips³⁶ (p.27), employing functional groups containing oxygen bonded to the silicon.^{13,30} For conciseness, their results are collected into the following diagram: ($R_3Si \equiv$ as above)



The reactions are numbered (i) to (vii) as shown. Reactions (ii) and (iv) must have been retentive, hence reactions (i) and (iii) were retentive and invertive, respectively. From this result it followed that reaction (vii) was also invertive.

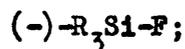
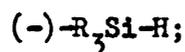
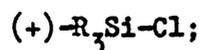
Cleavage of the disiloxane to the silanolate [reaction (v)], showed the cleavage to occur with retention of configuration,

while the preparation of (+)-silanolate from (-)-silanol [reaction(vi)] proved these two compounds to have the same configuration.

Sommer and Frye were therefore able to show that (using solid potassium hydroxide in xylene) methoxy- and methylphenyl-(α -naphthyl)siloxy- groups were displaced from silicon by hydroxyl, with retention of configuration; but that (under the same conditions) acetoxy- was replaced by hydroxyl with inversion of configuration. The displacement in pentane of acetoxy- by methoxy- was also invertive.

In order to include in this scheme the reactions involving methylphenyl(α -naphthyl)silane (p.28), Sommer, et al., employed physical methods of correlating sign of optical rotation with configuration: -^{15,30}

X-ray crystallography showed (R_3Si as above) that



all crystallised in the orthorhombic system and with the same space group, i.e., perfect isomorphism was observed. Further, all three possible binary mixtures of these enantiomers crystallised also in the same way, i.e., solid solutions were formed with random distribution of the substances. On the other hand, when ONE component of these binary mixtures was replaced by its enantiomer, a eutectic mixture was obtained, having no resemblance

to the previous crystal structure. Racemic mixtures also behaved as eutectics.

It was therefore inferred that the three enantiomers listed above were each of the same configuration, hence reduction of the chlorosilane (p.28) had taken place with inversion of configuration - not with retention as proposed earlier (p.28).

Unfortunately, the corresponding silanol was not obtained as a solid, and therefore could not be included in the above correlation, so a second physical method had to be employed: Optical rotatory dispersion measurements¹⁵ on the following compounds ($R_3Si \equiv$ as above):

- (+) $-R_3Si-Cl$;
- (-) $-R_3Si-F$;
- (-) $-R_3Si-H$;
- (-) $-R_3Si-OMe$;
- (-) $-R_3Si-OH$;
- (-) $-R_3Si-OCO.Me$;

showed them all to have very similar rotatory dispersion curves,³⁰ displaying negative Cotton effects at about the same wavelength (Figure 4). Of these enantiomers, the first three were believed (from the phase-difference method outlined above) to have the same configuration, while the remainder had been proved rigorously (by chemical methods, p.29) to have the same configuration. On this basis, Sommer and his co-workers inferred that all six enantiomers listed above had the same con-

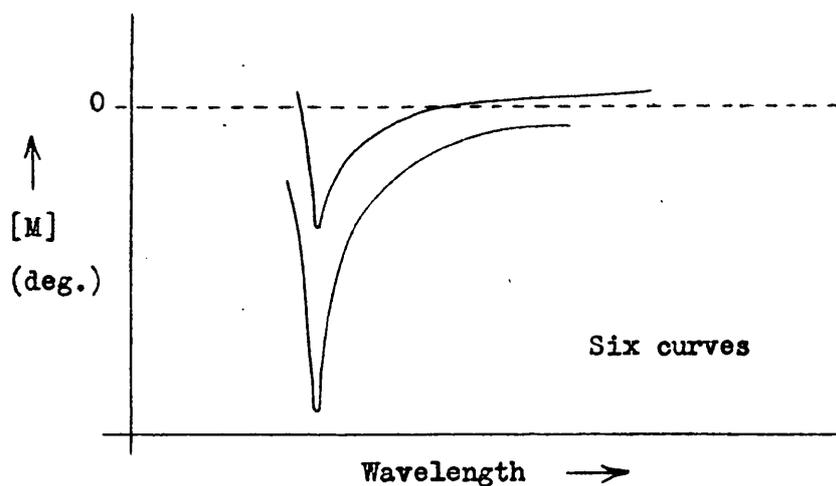
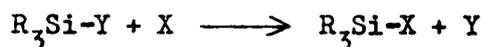


Fig. 4

figuration, and therefore deduced the predominant stereochemical path of some twenty reactions of the type (R_3Si as above):



where $Y = Cl, F, OH, OSiR_3, OCO.Me, OCO.CH_2Cl$;

$X = H, OMe, OCO.Me, Cl$.

Sommer pointed out that the stereochemical data could be summarised in terms of the leaving groups, of which he distinguished two types:^{15,30}

- (i) The "good leaving groups", such as Cl and OCO.R, whose conjugate acids have $pK_a < \sim 5$. These are the fairly-electro-negative groups, which are displaceable from carbon. All displacements at silicon of these groups involved INVERSION of configuration.
- (ii) The "poor leaving groups", such as H, OH, OMe, whose conjugate acids have $pK_a > \sim 10$. These are the more basic groups, which are not (usually) displaceable from carbon by nucleo-

philic reagents. Such displacements at silicon involved either INVERSION or RETENTION of configuration, in individual cases.

To rationalise his results, Sommer suggests³⁰ that there are two limiting bimolecular mechanisms for nucleophilic substitution at silicon:

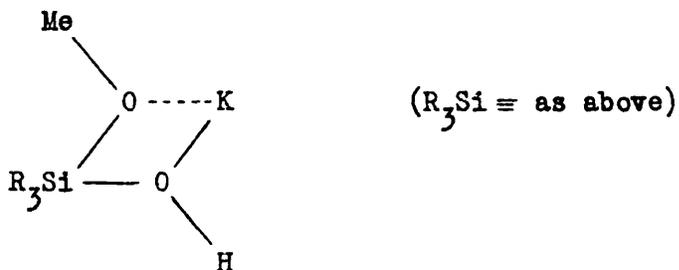
(I) A mechanism essentially similar to the carbon (S_N2) mechanism, involving a single transition state having three full bonds plus two highly stretched "bonds" joining the entering and leaving groups to the silicon atom. These three full bonds in the transition state may be "pure" sp^2 hybrids, or may use hybrid orbitals involving some contribution from the silicon 3d orbitals.

Hence INVERSION of configuration occurs for the same reason as with carbon, and such a mechanism might be expected to apply only to displacements known to occur at carbon, *i.e.*, to "good leaving groups".

(II) The other limiting bimolecular mechanism, Sommer designates the "expanded-octet" mechanism, and it is the mechanism described above (pp.20-25) in explaining the reactivity of silicon situated at a bridgehead.^{6,7,8} It is considered reasonable to assume a mechanism that is not available to carbon (but see page 18) for those displacements that do not occur at carbon. Sommer argues that displacement of "poor leaving groups" must require relative-

ly high activation of the silicon, and therefore very extensive electron-donation to the silicon by the attacking nucleophile, and that these requirements are best met by a mechanism in which full addition of the nucleophile to the silicon (with formation of five or six full bonds) must precede significant stretching of the bond between the silicon atom and the "poor leaving group".

With this mechanism, either INVERSION or RETENTION might occur, but whether the result is one or the other depends on "the relative importance of several factors",³⁰ which Sommer has not discussed at any length. He has however suggested¹³ that the "retentive" hydrolysis of methylphenyl(α -naphthyl)methoxysilane by solid potassium hydroxide in xylene (pp.29,30), was due to the poorly-ionising solvent favouring an S_Ni -like reaction of relatively undissociated complexes:



Transition state (cf. the Swain "push-pull" mechanism.⁴¹)

In aqueous acetone, the same reaction proceeded with inversion of configuration. Thus the methoxide could be converted into the silanol by either of two stereochemical paths; it seems that one

path may be encouraged and the other suppressed by varying the conditions sufficiently, echoing the duality of the S_N1 and S_N2 mechanisms in carbon chemistry.

EXPERIMENTALGeneral

(i) Hydrolysis of reaction mixtures obtained by coupling silicon-functional compounds with Grignard or organolithium reagents was effected by cautious addition (with stirring and cooling in ice) of water, or aqueous ammonium chloride solution. Dilute mineral acid was generally avoided because of the nature of the compounds involved. Solvent was removed from the solution eventually obtained via a short glass-helices packed column (1.4 x 30 cm.) when the required compound was silicon-functional; otherwise the solvent was stripped off via a Claisen head. The residue was fractionally distilled, usually at reduced pressure.

(ii) Fractional distillation of liquids at reduced pressure was achieved by distillation via a Vigreux column (0.7 x 52 cm.). Fractionations at atmospheric pressure were performed with a glass-helices packed column (1.2 x 70 cm.). Initially, the temperature of the electrically-heated jacket was set at ~ 5° below the boiling-point of the fraction being collected, but it was usually necessary (at pressures below ~ 1 mm.) to raise the jacket temperature to well above the boiling-point of the distillate in order to secure any distillation at all. Glass-wool or wooden "boiling-sticks" were used to produce even ebullition, and the still-pot was heated by means of either a silicone-oil bath or a heating mantle, according to the size of the flask.

(iii) Analyses for carbon and hydrogen were performed by

either Drs. Weiler and Strauss, 164, Banbury Rd., Oxford;
 or Dr. Bernhardt, Mulheim Ruhr, Kaiser Wilhelm Platz 1, W. Germany.
 Analyses for hydrolysable chlorine and fluorine were performed as
 follows:

Fluorine. The fluorosilane (~ 0.25 g.) was weighed into a stoppered weighing-bottle, then washed into a 250 ml. conical flask with alcohol (50 ml.). To the solution was added N/10 alcoholic sodium hydroxide solution (25 ml.), and the mixture titrated against standard N/10 aqueous potassium hydrogen phthalate solution, using phenolphthalein indicator. All solutions were carbon dioxide free. A blank, consisting of the same mixture less the fluorosilane, was also run. The difference ΔV between the two titrations represented the hydrolysable fluorine present:

$$\% \text{ F found} = \frac{\Delta V \times \text{Normality of K H Phthalate soln.} \times 19.00 \times 100}{1000 \times \text{wt. of fluorosilane}}$$

Chlorine. The chlorosilane (~ 0.25 g.) was weighed out as above, and dissolved in alcohol (25 ml.) in a stoppered 250 ml. conical flask. Water (50 ml.) was added, and the mixture shaken before titrating it against N/10 aqueous sodium hydroxide solution, using methyl red indicator. A blank consisting of standard N/10 sulphuric acid (25 ml.), water (25 ml.), and alcohol (25 ml.) was similarly titrated, to obtain the normality of the sodium hydroxide solution. Then

$$\% \text{ Cl found} = \frac{\text{Volume of NaOH soln. used} \times \text{Normality} \times 35.46 \times 100}{1000 \times \text{wt. of chlorosilane}}$$

(iv) Solvents, reagents, and starting materials were used as supplied except where indicated below:

Diethyl ether and benzene, for use in the preparation of Grignard and organolithium reagents and in lithium aluminium hydride reductions, were dried by contact with sodium wire for at least 24 hours.

Carbon tetrachloride was dried by fractional distillation, removing water as its azeotrope.

"Purified" petroleum spirit (b.p. below 40° , and b.p. $60-80^{\circ}$), the former designated herein as "pentane", were obtained by shaking petroleum spirit with concentrated sulphuric acid (3 times) until the acid was not discoloured, then rapidly distilling the petroleum spirit, and finally standing the petroleum spirit over sodium wire for at least 24 hours. Petroleum spirit undesigned as "purified" was not treated in any way.

Alcohol, as designated herein, contained 95% ethanol, 5% methanol, and was not purified before use.

Di-n-butyl ether was fractionally distilled from sodium: b.p. $141-2^{\circ}$ / 760 mm.

p-Bromoanisole was obtained from B.D.H., and used without further purification. It was also prepared by the method of Slotta and Heller⁴⁵ in 84% yield: b.p. $90-2^{\circ}$ / 12 mm.; n_D^{25} 1.5620. Lit: n_D^{20} 1.5640.

Isopropyl alcohol was purified by fractionation, collecting the fraction of b.p. 81.1° / 744 mm., which was refractionated from

calcium oxide: the middle cut had b.p. 81.1° / 765 mm.

Pyridine was allowed to stand over potassium hydroxide pellets for 24 hours, then fractionated, collecting the fraction of b.p. 113.9° / 727 mm., which was refractionated: the middle cut had b.p. 115° / 755 mm.

Cyclohexylamine was fractionated to obtain a middle cut having b.p. 133° / 756 mm.

Methanol was dried by the method of Lund and Bjerrum⁴⁶ i.e., by distillation from magnesium methoxide.

Methanol labelled with tritium in the methyl group was prepared from tritiated water by the method of Melander⁴⁷, described also by Swain and Pegues⁴⁸, and by Martin.³⁸

Methyltrichlorosilane (technical grade) was supplied by Hopkins and Williams, and used without purification.

Methyltriethoxysilane (technical grade) was supplied by Hopkins and Williams, and used without purification. It was also prepared from methyltrichlorosilane by the method of Tamborski and Post⁴⁹ in 52% yield: b.p. 144° / 760 mm., n_D^{25} 1.3815; lit⁴⁹: b.p. 144.5° / 760 mm., n_D^{25} 1.3811

PART ONE: The Preparation of Asymmetric Organosilicon Compounds
Containing the Arylethylmethylsilyl Group.

(A) The Preparation of (+)-p-[Ethylmethyl(p-methoxyphenyl)silyl]-
benzoic Acid

(i) Ethylmethyldichlorosilane²⁹.

Ethyl bromide (130.8 g., 1.2 mole) was reacted with magnesium turnings (28.8 g., 1.2 g. atoms) in a total of 400 ml. of ether, and refluxed for 2 hours. The dark grey solution was transferred to a dropping funnel containing a plug of glass-wool, and added dropwise, over 7 hours, to a solution of methyltrichlorosilane (150 g., 1.0 mole) in ether (50 ml.), cooled in ice. The mixture was distilled to dryness, the oil-bath temperature reaching 220°, and the distillate was fractionated to obtain the required product: 65.7 g., 45.9% (based on the methyltrichlorosilane), b.p. 100-2°. Lit⁶¹: b.p. 100.5°

(ii) Ethylmethyl(p-chlorophenyl)fluorosilane.

p-Bromochlorobenzene (129.2 g., 0.68 mole) was dissolved in ether (500 ml.) and reacted with magnesium turnings (16.4 g., 0.68 g. atom) in ether (50 ml.), cooled in ice. The mixture was refluxed for 3/4 hour, then added dropwise over 1 hour to a solution of ethylmethyldichlorosilane (87.8 g., 0.64 mole) in ether (200 ml.), cooled in ice. This mixture was refluxed for 3 hours before cooling in ice and hydrolysing with 2N hydrochloric acid. The ethereal solution was separated, washed

with water, and dried over anhydrous sodium sulphate. Solvent was stripped off via a Claisen head. The residue was dissolved in alcohol (1500 ml.), hydrofluoric acid (100 ml. of a 40% aqueous solution) was added, and the mixture heated on a water-bath at $\sim 60^\circ$ to redissolve precipitated material. The alcoholic solution was maintained at this temperature for 8 hours, during which time a further 4 x 100 ml. of aqueous hydrofluoric acid was added. The solution was poured into 5 litres of water and extracted with petroleum spirit (b.p. below 40°) (4 x 250 ml.). The latter was dried over anhydrous sodium sulphate, and fractionated to give the required ethylmethyl(p-chlorophenyl)fluorosilane, 37.0 g., 29.8% (based on the ethylmethyldichlorosilane), b.p. $90-4^\circ / 13$ mm., n_D^{20} 1.4984. (Found: F, 9.19. $C_9H_{12}ClFSi$ requires F, 9.37%)

(iii) Ethylmethyl(p-methoxyphenyl)chlorosilane.

p-Bromoanisole

(123.5 g., 0.66 mole) in ether (250 ml.) was reacted with magnesium turnings (16.0 g., 0.66 g. atom) in ether (100 ml.) and refluxed for $1\frac{1}{2}$ hours, before being added dropwise to a cooled solution of ethylmethyldichlorosilane (78.5 g., 0.55 mole) in ether (100 ml.). The mixture was refluxed for 2 hours, and left to settle overnight. The supernatant solution was decanted off under nitrogen, and the residual salts washed similarly with ether (4 x 150 ml.). The total ethereal solution thus obtained was distilled quickly at atmospheric pressure to remove ether, then at reduced pressure (up to $200^\circ / \sim 1$ mm.) to remove the chlorosilane from the magnesium salts. Finally,

the latter distillate was fractionated to give a main fraction, ethylmethyl(p-methoxyphenyl)chlorosilane, 20.1 g., b.p. 62-84° / ~ 1 mm. Acidimetric titration showed it to be 96% pure. A subsequent preparation gave a product of b.p. 116° / 5 mm., n_D^{20} 1.5173 (Found: Cl, 16.17. $C_{10}H_{15}ClOSi$ requires Cl, 16.52%.)

(iv) Methyl(p-bromophenyl)diethoxysilane.

p-Dibromobenzene (353.7 g., 1.5 mole), dissolved in ether (500 ml.) and benzene (500 ml.), was reacted with magnesium turnings (36.4 g., 1.5 g. atoms) in ether (100 ml.), with vigorous stirring and ice-cooling in order to add the halide solution as rapidly as possible. The resultant solution was stirred for 2 hours at room temperature, then to it was added rapidly a solution of methyltriethoxysilane (178 g., 1.0 mole) in ether (100 ml.). The mixture was refluxed for 8 hours. Cautious hydrolysis, using ammonium chloride solution, gave an ethereal solution which was worked up in the usual way to yield, on fractionation, the required compound, 121.4 g., 42% (based on the methyltriethoxysilane), b.p. 107° / 3 mm., n_D^{20} 1.5016. (Found: C, 45.85; H, 5.91. $C_{11}H_{17}BrO_2Si$ requires C, 45.68; H, 5.93 %.) Lit⁵¹: b.p. 87-8° / 2-3 mm., n_D^{25} 1.4980.

(v) Ethylmethyl(p-bromophenyl)ethoxysilane.

Two methods were employed:

Method (a) Ethyl bromide (96.4 g., 0.88 mole) was reacted with magnesium turnings (21.5 g., 0.88 g. atom) in ether (500 ml.), then

refluxed for 1 hour. To the cooled solution was added rapidly methyl(p-bromophenyl)diethoxysilane (221.0 g., 0.77 mole), the mixture was refluxed for 6 hours and then was left at room temperature overnight, when reaction occurred, producing much precipitate and a pale yellow supernatant liquid. The ether was distilled off and replaced by benzene, and the mixture cautiously hydrolysed by means of ammonium chloride solution. The benzene solution thus obtained was dried over anhydrous sodium sulphate and the solvent removed, before fractionation at reduced pressure to give ethylmethyl(p-bromophenyl)ethoxysilane, 164.0 g., 78.4 % (based on the diethoxysilane), b.p. 142° / 18 mm., n_D^{20} 1.5168. (Found: C, 48.56; H, 6.44. $C_{11}H_{17}BrOSi$ requires C, 48.35; H, 6.27 %)

Method (b) p-Dibromobenzene (425 g., 1.8 mole), dissolved in ether (1000 ml.) and benzene (500 ml.), was reacted with magnesium turnings (43.8 g., 1.8 g. atoms) in ether (200 ml.) cooled in an alcohol/Drikold bath at its lowest temperature (in order to add the halide solution as quickly as possible) once the reaction had begun. The mixture was allowed to warm up to room temperature and stirred for 1 hour, by which time almost all the magnesium had dissolved. The mixture was cooled in ice, and a solution of methyltriethoxysilane (267.4 g., 1.5 mole) in ether (100 ml.) added rapidly. The mixture was refluxed for 6 hours then cooled in ice before adding to it rapidly a solution of ethylmagnesium bromide prepared from ethyl bromide (196.2 g., 1.8 mole) and magnesium turnings (43.8 g., 1.8 g. atoms) in ether (800 ml.). The reaction mixture was allowed to

warm up to room temperature, and refluxed for 5 hours. After cautious hydrolysis by means of ammonium chloride solution, the solution was worked up as in method (a) above to give the required compound, 269 g., 65.6 % (based on the triethoxysilane), b.p. 118-124° / 6 mm., n_D^{20} 1.5172.

(vi) Ethylmethyl(p-bromophenyl)fluorosilane.

Using 2N hydrochloric

acid instead of ammonium chloride solution in the working up of ethylmethyl(p-bromophenyl)ethoxysilane (method (b), same quantities), and not removing the ethereal solution immediately from contact with the acidic aqueous solution, gave a very high-boiling residue (193.8 g.) on removal of the solvent. This residue was dissolved in alcohol (2000 ml.) and heated at ~ 60° on a water-bath, together with hydrofluoric acid (600 ml. of a 40 % aqueous solution), for 6 hours. The reaction mixture was poured into 6 litres of water, and extracted with petroleum spirit (b.p. 60-80°) (3 x 500 ml.), which was washed with water and dried over anhydrous sodium sulphate. The solvent was removed to give a residue (133 g.) which was fractionated to give ethylmethyl(p-bromophenyl)fluorosilane, 67.0 g., 18.1 % (based on the triethoxysilane), b.p. 232° / 764 mm., n_D^{20} 1.5161.

(Found: F, 7.57. $C_9H_{12}BrFSi$ requires F, 7.70 %.)

(vii) Ethylmethyl(p-chlorophenyl)(p-methoxyphenyl)silane.

p-Bromo-

anisole (50.5 g., 0.27 mole) in ether (100 ml.) was reacted, under nitrogen, with lithium metal (3.8 g., 0.54 g. atom) in ether (100 ml.)

(cooled in ice), then refluxed for two hours. The resultant solution was added dropwise to a solution of ethylmethyl(p-chlorophenyl)fluorosilane (36.5 g., 0.18 mole) in ether (100 ml.), and the mixture refluxed for 2 hours before hydrolysing it and working up the ethereal solution in the usual way. After removal of solvent, the residue was fractionated to give ethylmethyl(p-chlorophenyl)(p-methoxyphenyl)silane, much trouble being experienced from solid which appeared in the fractions:

Main fraction (cloudy), 26.4 g., b.p. 156-7° / 1-2 mm., n_D^{20} 1.5719.

Middle cut (α) (transparent), b.p. 156° / 1-2 mm., n_D^{20} 1.5713.

A sample recovered from preparation (ix) [below] gave:

Middle cut (β) (transparent), b.p. 157° / 1-2 mm., n_D^{20} 1.5722.

(Found for α : C, 65.75; H, 6.91. Found for β : C, 66.65; H, 6.19.

$C_{16}H_{19}ClOSi$ requires C, 66.08; H, 6.58 %.)

(viii) Ethylmethyl(p-bromophenyl)(p-methoxyphenyl)silane.

Two methods

were employed:

Method (a) n-Butyl chloride (11.9 g., 0.13 mole) was reacted under nitrogen with lithium metal (1.78 g., 0.26 g. atom) in ether (200 ml.) at ~ - 30°, with vigorous stirring. The mixture was allowed to warm up to ~ + 10°, then added dropwise, under nitrogen, with stirring and ice-cooling, to a solution of p-dibromobenzene (24.3 g., 0.1 mole) in ether (100 ml.), and finally refluxed for ½ hour. To the cooled reaction mixture was added dropwise, under nitrogen, and

with stirring, a solution of ethylmethyl(p-bromophenyl)chlorosilane (20.1 g., 0.094 mole) in ether (50 ml.). The mixture was refluxed for 2 hours before adding benzene (200 ml.) and distilling off the ether. The mixture was filtered, the benzene stripped off, and the residue fractionated to give ethylmethyl(p-bromophenyl)(p-methoxyphenyl)silane, 16.3 g., 52 % (based on the chlorosilane), b.p. 168° / 3 mm., n_D^{20} 1.5860. (Found: C, 57.51; H, 5.86.

$C_{16}H_{19}BrOSi$ requires C, 57.31; H, 5.71 %.)

Method (b) p-Bromoanisole (280.5 g., 1.5 mole) was reacted under nitrogen with lithium metal (20.8 g., 3.0 g. atoms) in ether (750 ml.), which was stirred vigorously and cooled in ice. The resultant solution was added rapidly to a solution of ethylmethyl(p-bromophenyl)ethoxysilane (269 g., 0.98 mole) in ether (50 ml.) cooled in cold water. The mixture was stirred for 1 hour, then left at room temperature for ~ 70 hours, when it was poured onto crushed ice. Dilute hydrochloric acid was added cautiously until two clear layers were obtained, and the ethereal solution worked up as usual. Fractionation gave the required compound, 227 g., 69 % (based on the ethoxysilane), b.p. 192° / 4 mm., n_D^{20} 1.5865.

(ix) p-[Ethylmethyl(p-methoxyphenyl)silyl]benzoic acid.

Two methods

were tried:

Method (a) A solution of ethylmethyl(p-chlorophenyl)(p-methoxyphenyl)silane (26.4 g., 0.09 mole) in ether (100 ml.) was added slowly, with vigorous stirring, to lithium metal (1.6 g., 0.23

g. atom) in ether, under nitrogen. The reaction proceeded with difficulty and with scarcely any evolution of heat. After 3 hours, the brown mixture was gently refluxed (with stirring) for $1\frac{1}{2}$ hours, then stirred without heating for a further 2 hours. The resultant solution was transferred to a 500 ml. dropping funnel, and added dropwise to a large excess of crushed Drikold. When the excess Drikold had evaporated, the ethereal residue was acidified with dilute hydrochloric acid. The ether solution was separated, washed with water, then with dilute sodium hydroxide solution, then again with water, and dried over anhydrous sodium sulphate. Removal of solvent gave an oil (17.6 g.) which was fractionated:

Forerun, ~ 0.5 g., b.p. 20-140° / 1-2 mm., n_D^{20} 1.5504

Fraction I, 3.6 g., b.p. 140-150° / 1-2 mm., n_D^{20} 1.5655

Fraction II, 9.6 g., b.p. 150-158° / 1-2 mm., n_D^{20} 1.5713

Fraction II was presumed to be starting material, and was re-fractionated to obtain a sample for analysis -- see (vii), above.

The aqueous sodium hydroxide extract (above) was washed with ether before acidifying with dilute hydrochloric acid and extracting the resultant "emulsion" with ether. The ethereal solution thus obtained was washed with water (3 times), dried over anhydrous sodium sulphate, and the solvent removed to give a brown oil (5.2 g.) which could not be crystallised from petroleum spirit (b.p. 60-80°), or from aqueous alcohol.

Method (b) Ethylmethyl(p-bromophenyl)(p-methoxyphenyl)silane (189 g., 0.56 mole) was reacted with magnesium turnings (15.0 g., 0.62 g.

atom) in ether (300 ml.), under nitrogen; then the mixture was refluxed gently for 2 hours. The cooled mixture was diluted with ether (200 ml.) before being poured slowly onto a Drikold/ether slurry which was then allowed to attain room temperature overnight. Water (1500 ml.) was added to give 2 clear layers, and the mixture transferred to a 5 litre separatory funnel where it was cautiously acidified (as shown by B.D.H. Wide Range test papers) by means of 2N sulphuric acid. The aqueous layer was removed, and the yellow ethereal solution washed 3 times with water, then extracted with N sodium hydroxide solution (2 x 1000 ml.). The combined alkaline extracts were washed 3 times with ether, then ether (1000 ml.) was added, and the mixture carefully acidified (shaking it at intervals) with 2N sulphuric acid. The bright-yellow ethereal solution thus obtained was washed 3 times with water and dried over anhydrous sodium sulphate. The solvent was removed at reduced pressure to leave the p-[ethylmethyl(p-methoxyphenyl)silyl]benzoic acid as an off-white solid (115.5 g., 68 %) which was recrystallised 4 times from petroleum spirit (b.p. 60-80°): m.p. 106-7°. Recrystallisation twice from aqueous alcohol gave m.p. 106.5-107.0°. (Found: C, 67.85; H, 6.72. $C_{17}H_{20}O_3Si$ requires C, 67.97; H, 6.71 %.)

(B) The Resolution of (+)-p-[Ethylmethyl(p-methoxyphenyl)silyl]-benzoic Acid

(i) The preparation and separation of the (-)-quinine diastereoisomeric salts of the racemic acid.

A solution of (+)-p-[ethylmethyl(p-methoxyphenyl)silyl]benzoic acid (120.5 g., 0.40 mole) in alcohol (250 ml.) was added to a solution of (-)-quinine (135 g., 0.42 mole) in alcohol (750 ml.), and the resultant salt allowed to crystallise. The quinine salt was filtered off, washed with alcohol, then recrystallised a further 6 times from alcohol, to constant melting point: m.p. 194-7° (dec.), $[\alpha]_D - 121.8^\circ$ in chloroform (c, 1.10).

(ii) The regeneration of (+)-p-[ethylmethyl(p-methoxyphenyl)silyl]benzoic acid from its (-)-quinine salt.

The sparingly-soluble diastereoisomeric salt (25.0 g.) was placed in a 1 litre separatory funnel, together with ether (400 ml.) and water (300 ml.). Dilute (N/10) hydrochloric acid was added in portions until all solid dissolved on vigorously shaking the mixture. The ethereal solution was separated, washed 3 times with water, and dried over anhydrous sodium sulphate, before removing the solvent at reduced pressure to leave a white solid (12.3 g.). Recrystallisation from aqueous alcohol gave the required acid, 9.8 g., m.p. 106-7°, $[\alpha]_D 1.2^\circ$ in benzene (c, 3.68).

(C) An Attempt to Decarboxylate (+)-p-[Ethylmethyl(p-methoxyphenyl)silyl]benzoic Acid

(+)- acid (1.0 g.) was ground up with soda-lime (6.0 g.) and placed in a pyrex test-tube having a 90° bend and fitted with a delivery

tube into another test-tube. The powdered solid was covered with more soda-lime, and the mixture heated slowly until it was red hot. The distillate separated into two layers. The bright-yellow upper layer (~ 0.5 ml.) was separated from the cloudy aqueous layer, and its boiling point determined by the usual micro method: b.p. 150° and 152° successively, hence it was concluded that the principal product was anisole (b.p. 154°).

- (D) The Preparation of Optically-Active Non-Silicon-Functional Derivatives of (+)-p-[Ethylmethyl(p-methoxyphenyl)silyl]benzoic Acid
- (i) Methyl p-[ethylmethyl(p-methoxyphenyl)silyl]benzoate.

(a) From

racemic acid. In a 500 ml. 3-necked flask, fitted with stirrer and Liebig condenser, was placed potassium hydroxide (25 g.), water (100 ml.), and ether (150 ml.). This mixture was cooled in ice-salt mixture and stirred while α -methyl-N-nitrosourea⁵² (30 g.) was added down the condenser, in portions, over ~ 1½ hours,⁵³ maintaining the temperature below 5°. The contents of the flask was transferred to a chilled 500 ml. separatory funnel, the aqueous layer removed, and the bright-yellow ethereal layer washed twice with cold water, before drying it over anhydrous sodium sulphate for ~ 5 minutes. The filtered solution was used immediately for methylating the (+)-acid:

To the above ethereal solution of diazomethane was added, in portions, excess (+)-acid (18.4 g., 0.06 mole). Dilute hydrochloric

acid was then added to ensure complete removal of excess diazomethane. The mixture was washed with dilute sodium hydroxide solution to remove excess (+)-acid, then with water (3 times), and dried over anhydrous sodium sulphate. Removal of solvent at reduced pressure gave a yellow oil (16.2 g., 84 % based on the (+)-acid), which was fractionated to give methyl p-[ethylmethyl(p-methoxyphenyl)silyl]benzoate, b.p. 168° / 0.05 mm., n_D^{20} 1.5658, n_D^{25} 1.5632. (Found: C, 68.63; H, 6.94. $C_{18}H_{22}O_3Si$ requires C, 68.77; H, 7.06 %.)

(b) From

(+)-acid. By the same method as above, (+)-p-[ethylmethyl(p-methoxyphenyl)silyl]benzoic acid (44.4 g., 0.15 mole) was methylated to yield a cloudy yellow oil (42.8 g., 92 %), which was fractionated: the required compound had b.p. 183° / 0.1 mm., n_D^{25} 1.5632, $[\alpha]_D - 0.16^\circ$ in carbon tetrachloride (c, 40.0).

(ii) p-[Ethylmethyl(p-methoxyphenyl)silyl]benzyl alcohol.

(a) From

racemic acid⁵⁴. Lithium aluminium hydride (7.0 g., 0.18 mole) and ether (400 ml.) were placed in a 1 litre 3-necked flask fitted with stirrer, condenser, dropping funnel, and guard-tubes. The mixture was stirred and refluxed gently for 1 hour, then cooled to room temperature. To the resultant slurry was added dropwise a solution of (+)-p-[ethylmethyl(p-methoxyphenyl)silyl]benzoic acid (36.8 g., 0.12 mole) in ether (200 ml.). The mixture was refluxed for 3 hours, then left at room temperature overnight before it was hydrolysed with water, transferred to a separatory funnel and cautiously

acidified with 2N sulphuric acid. The aqueous layer was removed and washed with ether. The combined ether layers were extracted with 2N sodium hydroxide solution, washed twice with water, and dried over anhydrous sodium sulphate. The solvent was stripped off and the residue fractionated to give four slightly-cloudy fractions of constant boiling point and refractive index: b.p. 168° / 0.01 mm., n_D^{25} 1.5733. These distillates were added to more alcohol obtained from a similar preparation, using 28.7 g., 0.095 mole, of (+)-acid, and the whole fractionated. Cloudy fractions (total weight 53.1 g., 85 % (based on the substituted benzoic acid)) of constant boiling point and refractive index, b.p. 183° / 0.02 mm., n_D^{25} 1.5737, were obtained.

(b) From

(+)-acid. Lithium aluminium hydride (10.0 g., 0.26 mole) in ether (450 ml.) was reacted, as above, with (+)-p-[ethylmethyl(p-methoxy-phenyl)silyl]benzoic acid (80.9 g., 0.27 mole) in ether (200 ml.). [From the aqueous sodium hydroxide extract of the reaction mixture was obtained (on acidification, etc.) a white solid (8.6 g.) which was recrystallised from aqueous alcohol: 7.2 g., m.p. $105.5-107.0^{\circ}$. I.e., unchanged (+)-acid.] Fractionation of the product gave four slightly cloudy fractions (total weight 64.1 g., 83 %) having constant boiling point and refractive index: b.p. 167° / 0.02 mm., n_D^{25} 1.5735. The clearest fraction was taken to be p-[ethylmethyl-(p-methoxyphenyl)silyl]benzyl alcohol, 12.5 g., $[\alpha]_D$ 0.14° in benzene (c, 38.2). (Found: C, 71.50; H, 7.85. $C_{17}H_{22}O_2Si$ requires

C, 71.29; H, 7.74 %.)

(iii) p-[Ethylmethyl(p-methoxyphenyl)silyl]benzyl methyl ether.

(a) From

racemic alcohol. Sodium (4.8 g., 0.21 mole) and toluene (200 ml.) were placed in a 1 litre 3-necked flask fitted with stirrer, condenser, and dropping funnel. The toluene was brought to reflux, and the mixture stirred vigorously to disperse the molten sodium. A solution of (+)-p-[ethylmethyl(p-methoxyphenyl)silyl]benzyl alcohol (47.4 g., 0.17 mole) in toluene (100 ml.) was added. No precipitate was formed, but the solution became yellow. The mixture was stirred and refluxed for 75 minutes, and the heating mantle removed before adding dimethyl sulphate (22.0 g., 0.18 mole) to the hot solution. A very vigorous reaction occurred, with the formation of a white gelatinous precipitate. The mixture was refluxed for 75 minutes, then stirred for 30 minutes without heating. To the mixture, cooled in ice, was added methanol (100 ml.) to remove the excess sodium, then concentrated ammonia solution (250 ml.) to destroy excess dimethyl sulphate. The mixture was worked up as usual, to give an ether-toluene solution, which was dried over anhydrous sodium sulphate. The solvent was removed rapidly, and the residue fractionated; the main fraction had b.p. 150-160° / 0.04 mm., n_D^{25} 1.5560, wt. 26.4 g. (51.7 %, based on the substituted benzyl alcohol). The infrared spectrum indicated the absence of hydroxyl. Refractionation gave seven fractions of very similar boiling points and refractive indices; the middle cut had

b.p. 148-150° / 0.05 mm., n_D^{25} 1.5555. The latter (10.9 g.), on fractionation, gave five fractions of constant boiling point and refractive index; the middle cut was taken to be the required p-[ethylmethyl(p-methoxyphenyl)silyl]benzyl methyl ether, 4.2 g., b.p. 172° / 0.07 mm., n_D^{25} 1.5563 (Found: C, 71.65; H, 7.94. $C_{18}H_{24}O_2Si$ requires C, 71.94; H, 8.05 %.)

(b) From

(+)-alcohol. Sodium (7.2 g., 0.3 mole) was dispersed in refluxing xylene, and reacted with (+)-p-[ethylmethyl(p-methoxyphenyl)silyl]-benzyl alcohol (58.0 g., 0.20 mole) in xylene (100 ml.), as in (a). The mixture was refluxed for 6 hours, with stirring, then left to cool to room temperature overnight, by which time some white solid had precipitated. Methyl iodide (50 g., 0.35 mole) was added, the mixture allowed to stand at room temperature for 5 days, then worked up as above (without addition of ammonia solution). Fractionation, twice, of the product gave a middle fraction having wt. 35.9 g., 59.7 % (based on the (+)-alcohol), b.p. 152-6° / 0.04 mm., n_D^{25} 1.5565, $[\alpha]_D - 0.19^\circ$ in benzene (c, 40.24), $[\alpha]_D - 0.25^\circ$ in carbon tetrachloride (c, 40.13).

(E) The Attempted Preparation of Optically-Active Silicon-Functional
Compounds Containing the Arylethylmethylsilyl Group

(i) p-(ethylmethylisopropoxysilyl)benzoic acid.

(+)-p-[Ethylmethyl-(p-methoxyphenyl)silyl]benzoic acid (5.0 g., 0.017 mole) was diss-

olved in carbon tetrachloride (50 ml.), and a solution of bromine (2.7 g., 0.017 mole) in carbon tetrachloride (10 ml.) added rapidly. Much heat was evolved. Since the solution was still coloured after 3 hours, it was left overnight. Solvent, together with some p-bromoanisole, was removed at reduced pressure (down to 1 mm.), and then purified petroleum spirit (b.p. 60-80°) (100 ml.) was added. The solution thus obtained was added rapidly to a swirled mixture of isopropyl alcohol (7 ml.) and cyclohexylamine (3.5 ml.) in purified petroleum spirit (200 ml.). Water (400 ml.) was added and the mixture shaken vigorously and separated; the upper layer was washed again with water (3 times), and dried over anhydrous sodium sulphate. [Some solid (α) in the interface of the second washing was removed by filtration, and recrystallised from benzene / petroleum spirit (b.p. 60-80°): m.p. 187-188°. A Lassaigne test on α showed nitrogen to be absent. The mixed melting point of α with a sample of sym-di(p-carboxyphenyl)diethyldimethyldisiloxane²⁹ (m.p. 216-218°) was 140-183°. Recrystallisation of α , twice, from benzene / petroleum spirit changed its melting point successively to 183-193° and 178-194°.] The sodium sulphate-dried solution was evaporated down to yield a sticky yellow solid (β), which on refluxing with benzene gave an insoluble residue (γ) of m.p. 270-300° (dec.). Attempts to recrystallise γ were unsuccessful since it was apparently insoluble in all solvents tried, e.g., chloroform, acetone, benzene, and absolute alcohol. The benzene solution of β gave no precipitate on adding petroleum spirit (b.p. 60-80°), and evaporation of the solvent

gave only an extremely small amount of a flocculent solid (~ 0.1 g.). The authentic cyclohexylamine - (+)-acid salt was prepared from a solution of (+)-acid in the minimum of carbon tetrachloride, to which excess cyclohexylamine was added, followed by a large excess of petroleum spirit (b.p. $60-80^\circ$). The solution deposited the required salt on standing it at room temperature for 24 hours; the salt was filtered off and recrystallised from benzene / petroleum spirit: m.p. 147° . The authentic cyclohexylamine salt of sym-di(p-carboxyphenyl)diethyl dimethyl disiloxane was similarly prepared, employing disiloxane of m.p. $216-8^\circ$. The melting point of the crude salt was $190-223^\circ$; its mixed melting point with the disiloxane was $159-180^\circ$.

Repeat experiments gave similar intractable solids (generally of very indeterminate melting point) none of which resembled the starting acid, the related disiloxane, or their cyclohexylamine salts.

(ii) A semi-quantitative investigation of the stereochemistry of bromine-cleavage of (-)-methyl p-[ethylmethyl(p-methoxyphenyl)-silyl]benzoate.

Bromine (12.526 g.) was weighed into a graduated flask, and the volume made up to 25 ml. by means of dry carbon tetrachloride.

Optically-active methyl ester (2.1 g., 0.0064 mole) was placed in a 2 dm. centre-filling polarimeter tube, and dissolved in dry carbon tetrachloride (~ 15 ml.). The observed rotation was $\alpha =$

- $0.02^\circ \pm 0.005$. To the optically-active solution was added 1.50 ml. of the above bromine solution, i.e., 0.75₁ g. (0.0047 mole) of bromine. The rotation of the solution, when the bromine colour had cleared sufficiently (~ 20 minutes), was $\alpha = + 0.08^\circ \pm 0.01$. After 7 hours at room temperature, the rotation was $\alpha = + 0.02^\circ \pm 0.005$; this value remaining constant for 7 days.

(iii) Methyl p-(ethylmethyloisopropoxysilyl)benzoate.

(a) From the

optically-active methyl ester. (-)-Methyl ester (p. 50) (0.87 g., 0.0028 mole) was weighed into a test-tube and dissolved in purified petroleum spirit (b.p. 60-80°) (5 ml.). To the solution was added a solution of bromine (0.0028 mole) in purified petroleum spirit. The bromine colour disappeared within 15 minutes. To this solution was added a solution of isopropyl alcohol (0.0028 mole) and pyridine (0.0028 mole) in purified petroleum spirit (1.8 ml.). An immediate white precipitate was formed. The mixture was well shaken, filtered at the pump, and the precipitate washed with purified petroleum spirit (15 ml.). The filtrate was refiltered twice to remove further precipitate, then poured into a 2 dm. polarimeter tube. The observed rotation was $\alpha = 0.00^\circ \pm 0.005$.

(b) From the

racemic ester. (+)-Methyl p-[ethylmethyl(p-methoxyphenyl)silyl]-benzoate (12.6 g., 0.04 mole) was dissolved in carbon tetrachloride (15 ml.) and cooled in cold water while a solution of bromine (5.59 g., 0.035 mole) in carbon tetrachloride (25 ml.) was added

rapidly. The solution was stood in the dark for 30 minutes, then diluted with purified petroleum spirit (b.p. 60-80°) (50 ml.). The resulting solution was added rapidly to a solution of isopropyl alcohol (14 ml.) and cyclohexylamine (7 ml.) in purified petroleum spirit, and the whole shaken thoroughly. Water (200 ml.) was added and the mixture again vigorously shaken. The petroleum spirit layer was separated, washed similarly 4 times with water, and dried over anhydrous sodium sulphate for 1 hour. The solvent was removed under reduced pressure to yield a slightly yellow oil (19.2 g.) which smelled of cyclohexylamine and contained fine white solid in suspension. This oil was diluted with petroleum spirit (b.p. 60-80°) (300 ml.), filtered*, and the solvent removed as before to give an oil that still contained suspended solid. The oil was redissolved in petroleum spirit (300 ml.) and washed with water (2 x 500 ml.), redried over anhydrous sodium sulphate, and the solvent removed as above, to give a cloudy residue (17.4 g.) which was apparently free of solid. This residue was fractionated:
Fraction I, 5.4 g., b.p. 83-89° / 8 mm., cloudy in early stages.

Odour of p-bromoanisole.

Fraction II, 6.8 g., b.p. 152° / 8 mm., transparent.

The latter fraction was added to that obtained similarly from 12.2 g. of (+)-ester, and the whole refractionated to give the required methyl p-(ethylmethylisopropoxysilyl)benzoate, 9.2 g., b.p. 152° / 8-9 mm., n_D^{25} 1.4919. (Found: C, 63.19; H, 8.18. $C_{14}H_{22}O_3Si$ requires C, 63.11; H, 8.32 %.)

[*The filtered off solid gave a positive reaction for ionisable halogen, and had m.p. 206-7°. Cyclohexylamine hydrobromide is⁶⁰ reported to have m.p. 195°]

(c) From the
optically-active methyl ester. (-)-Methyl p-[ethylmethyl(p-methoxy-phenyl)silyl]benzoate (10.0 g., 0.032 mole) was treated as above, the petroleum spirit solution being dried over anhydrous sodium sulphate for only 20 minutes. The solvent was removed at reduced pressure (water-bath below 35°) until the total volume was ~ 30 ml., when the solution was filtered. The solution was then reduced to a volume of ~ 25 ml., at reduced pressure, and poured into a 2 dm. polarimeter tube. Owing to the yellowness of the solution, the rotation was difficult to measure, but it was of the order of + 0.07-0.1°. The solution was evaporated down to give a cloudy yellow oil (14.0 g.), which was fractionated:

Fraction I, 5.0 g., b.p. 40-152° / 8 mm., very cloudy.

Fraction II, 3.1 g., b.p. 152-3° / 8 mm., contained solid.

The latter fraction was diluted with carbon tetrachloride (17 ml.), and poured into a 2 dm. polarimeter tube; the observed rotation was $\alpha = 0.00^\circ \pm 0.005$. The residue from the distillation (4.6 g.) was made up to 17 ml. with petroleum spirit (b.p. 60-80°): the observed rotation was $\alpha = + 0.125^\circ \pm 0.01$.

(d) From the
optically-active methyl ester. (-)-Methyl p-[ethylmethyl(p-methoxy-phenyl)silyl]benzoate (9.5 g., 0.030 mole) was treated as in (c),

above, to give a clear yellow solution (in petroleum spirit) (volume ~ 25 ml.), having a rotation $\alpha = + 0.07^\circ \pm 0.01$ in a 2 dm. polarimeter tube. This rotation was stable over 15 hours.

The solvent was removed at reduced pressure, and the cloudy yellow residue distilled as rapidly as possible, in a micro-distillation apparatus, by immersing the still-pot in a preheated silicone-oil bath:

Fraction I, ~ 6 ml. of clear distillate.

Fraction II, ~ 5 ml. of cloudy distillate.

Each "fraction" was made up to 17 ml. with petroleum spirit (b.p. 60-80°). The observed rotation of Fr. I, in a 2 dm. tube, was $\alpha = 0.00^\circ \pm 0.005$. The rotation of Fr. II was $\alpha = 0.015^\circ \pm 0.005$. The residue from the distillation (0.8 g.) was similarly diluted with petroleum spirit to ~ 17 ml.: the observed rotation was $\alpha = 0.08^\circ \pm 0.01$.

Authentic (-)-ester (0.8 g.) was placed in the 2 dm. polarimeter tube, and made up to ~ 17 ml. with petroleum spirit. The observed rotation was $\alpha = 0.00^\circ \pm 0.005$.

(iv) A semi-quantitative investigation of the stereochemistry of bromine-cleavage of (-)-p-[ethylmethyl(p-methoxyphenyl)silyl]-benzyl methyl ether.

Optically-active methyl ether (2.1 g., 0.0070 mole) was placed in a 2 dm. centre-filling polarimeter tube, and dissolved in dry carbon tetrachloride (~ 15 ml.). The observed rotation was $\alpha = - 0.02^\circ \pm 0.005$. To the optically-active solution

was added 2.0 ml. of the bromine solution employed in (ii), above (p. 56), i.e., 1.00 g. (0.0063 mole) of bromine. The rotation of the solution, when the bromine colour had cleared sufficiently (~ 20 minutes), was $\alpha = + 0.01^\circ \pm 0.01$. After 60 minutes, the rotation was $\alpha = + 0.02^\circ \pm 0.005$; the latter value remained constant for 6 days.

(v) p-(Ethylmethylsilyl)benzyl methyl ether.

(a) From the racemic

methyl ether. (+)-p-[Ethylmethyl(p-methoxyphenyl)silyl]benzyl methyl ether (15.2 g., 0.051 mole) in dry carbon tetrachloride (100 ml.) was placed in a 3-necked 250 ml. flask fitted with dropping funnel, stirrer, reflux condenser, and guard tubes. Bromine (7.3 g., 0.046 mole) in carbon tetrachloride (60 ml.) was added dropwise over 5 hours to the above ice-cooled solution, at such a rate as to maintain a yellow coloration, which disappeared on allowing the solution to stand overnight at room temperature. The solvent was removed at reduced pressure (water-bath below 45°), and the residual yellow oil was diluted with dry ether. To this solution was added cautiously a slurry of lithium aluminium hydride (2.0 g., 0.053 mole) in ether (100 ml.), and the mixture refluxed for 3 hours. Cyclohexane (100 ml.) was added, the diethyl ether fractionated off via a short glass-helices packed column, and acetone added carefully to decompose the excess lithium aluminium hydride. A further quantity of cyclohexane (50 ml.) was added, and the resultant mixture was poured into a separatory funnel containing concentrated hydro-

chloric acid (22 ml.) and crushed ice. The mixture was worked up as usual, to give a cyclohexane solution which was dried over anhydrous sodium sulphate. Solvent was removed at reduced pressure to leave a residue which was fractionally distilled:

Fraction I, 5.85 g., b.p. 40-92° / 8 mm., odour of p-bromoanisole.

Fraction II, 5.75 g., b.p. 130-6° / 20 mm.

Fraction III, 0.80 g., b.p. 138-140° / 10 mm.

Infrared spectra showed Fr. II to contain Si - H bonds, and Fr. III to contain, also, O - H bonds (i.e., absorption at 2100 cm^{-1} , and 3300 cm^{-1} , respectively).

(b) From the optically-active methyl ether. (α) (-)-p-[Ethylmethyl(p-methoxyphenyl)silyl]-benzyl methyl ether (10.05 g., 0.033 mole) was treated with bromine (4.8 g., 0.030 mole) exactly as in (a), above, to give ultimately a residue having a rotation $\alpha = + 0.1^\circ \pm 0.02$, in cyclohexane solution, in a 2 dm. polarimeter tube.

(β) (-)-Methyl ether (9.90 g., 0.033 mole) was treated with bromine (4.8 g., 0.030 mole) as in (a), above, except that the diethyl ether used was dried by distillation from lithium aluminium hydride, in addition to having been in contact with sodium wire. The final solution (30 ml.) had a rotation of $\alpha = + 0.08^\circ \pm 0.02$, in a 2 dm. polarimeter tube.

(γ) (-)-Methyl ether (10.20 g., 0.034 mole) was treated with bromine (4.9 g., 0.031 mole) as in (a), above, except that "pentane" was employed instead of carbon tetrachloride

throughout, to obviate the necessity for removing solvent before the addition of the lithium aluminium hydride slurry. The bromination reaction was slower than when carbon tetrachloride was used, but was nevertheless completed in 7 hours. The final solution (20 ml.) had a rotation of $\alpha = + 0.12^\circ \pm 0.02$, in a 2 dm. polarimeter tube.

The residues from the reactions (α), (β), and (γ), were combined and fractionally distilled:

Fraction I, 1.55 g., b.p. 40-90° / 16 mm., n_D^{25} 1.5150*

Fraction II, 10.15 g., b.p. 90-120° / 16-20 mm., n_D^{25} 1.5575**

Fraction III, 9.30 g., b.p. 120-130° / 20 mm., n_D^{25} 1.5039

Fraction IV, 3.10 g., b.p. 130-146° / 20 mm., n_D^{25} 1.5160

Residue = A

* n_D^{20} for anisole = 1.5179; ** n_D^{25} for p-bromoanisole = 1.5620

Each fraction was made up to 17 ml. with cyclohexane, and its rotation measured: all fractions were optically-inactive. Fractions III and IV were combined and refractionated at 20 mm.:

Fraction 1, 0.60 g., b.p. 40-80°, n_D^{25} 1.5030

Fraction 2, 2.00 g., b.p. 80-110°, n_D^{25} 1.5059

Fraction 3, 2.65 g., b.p. 110-130°, n_D^{25} 1.5038

Fraction 4, 0.25 g., b.p. 130°, n_D^{25} 1.4982

Fraction 5, 3.10 g., b.p. 130-136°, n_D^{25} 1.5010

Fraction 6, 0.75 g., b.p. 136-146°, n_D^{25} 1.4998

Infrared spectra showed all the fractions 1-6, inclusive, to contain Si - H and O - H bonds, but only fractions 3 and 4 had the

"ether band" (at 1090 cm^{-1}), similar to the starting material.

Fractions 2-5, inclusive, were combined and refractionated at 20 mm.:

Fraction 1A, 1.10 g., b.p. $90-5^\circ$, n_D^{25} 1.5034
Fraction 2A, 0.60 g., b.p. $95-102^\circ$, n_D^{25} 1.5027
Fraction 3A, 0.95 g., b.p. $102-112^\circ$, n_D^{25} 1.5155
Fraction 4A, 0.55 g., b.p. $112-122^\circ$, n_D^{25} 1.5115
Fraction 5A, 0.95 g., b.p. $122-132^\circ$, n_D^{25} 1.4975
Fraction 6A, 1.60 g., b.p. $132-140^\circ$, n_D^{25} 1.5021
Residue, 1.65 g., n_D^{25} 1.5049

Infrared spectra of fractions 6A and 5 (p. 63) were very similar, as were the spectra of fractions 5A and 4.

(Found for 2A: C, 68.23; H, 9.31. Found for 3A: C, 62.51; H, 7.54.

Found for 5A: C, 67.87; H, 9.34. $C_{11}H_{18}OSi$ requires C, 67.99;

H, 9.33 %.) In view of the infrared spectra of fractions 2A, 3A, and 5A (given on p. 67), fraction 5A was taken to be the required p-(ethylmethylsilyl)benzyl methyl ether.

The residue A from the first fractionation (p. 63) was filtered, and diluted to 75 ml. with diethyl ether. The rotation in a 2 dm. polarimeter tube was $\sim 0.1^\circ \pm 0.02$. This residue A was distilled in a microdistillation apparatus, via a Claisen head, at 0.02 mm.:

Fraction I, 1.05 g., pot-temperature 140° , n_D^{25} 1.5271
Fraction II, 0.30 g., " " 160° , n_D^{25} 1.5268
Fraction III, 2.70 g., " " 190° , n_D^{25} 1.5364

Fraction IV, 1.10 g., pot temperature 260°, n_D^{25} 1.5352

Residue B, 1.55 g., - -

All fractions were yellow. The infrared spectra of fractions I and II were identical, showing strong O - H and Si - H absorption bands, but no "ether band" (p. 64). The spectra of fractions III and IV, and of the residue B, were very similar, showing progressively weaker O - H and Si - H bands, but also complicated bands in the region 1000-1100 cm^{-1} , probably due to Si - O - Si. The rotation of B, when the latter was diluted to 75 ml. with diethyl ether, was $\sim 0.05^\circ$ in a 2 dm. tube.

Fractions I and II were combined: their rotation was $0.00^\circ \pm 0.005$ in a 1 dm. tube (no solvent). Fraction III had a rotation of $+ 0.92^\circ \pm 0.005$ in a 1 dm. tube (no solvent); it was combined with fraction IV, and redistilled as above, at 0.02 mm.:

Fr. 1, 0.15 g., pot temp. 180-200°, head temp. 80-140°, n_D^{25} 1.5315

Fr. 2, 2.30 g., " " 200-212°, " " 140-160°, n_D^{25} 1.5372

Fr. 3, 0.45 g., " " 212-220°, " " 160-60°, n_D^{25} 1.5361

All fractions were faintly yellow. Infrared spectra showed that fraction 1 contained much OH and SiH, but that fractions 2 and 3 were seemingly identical, with little OH and SiH.

Fractions 2 and 3 were combined and redistilled at 0.02 mm.:

Fraction 1A, 0.35 g., pot temperature 170-180°, n_D^{25} 1.5367

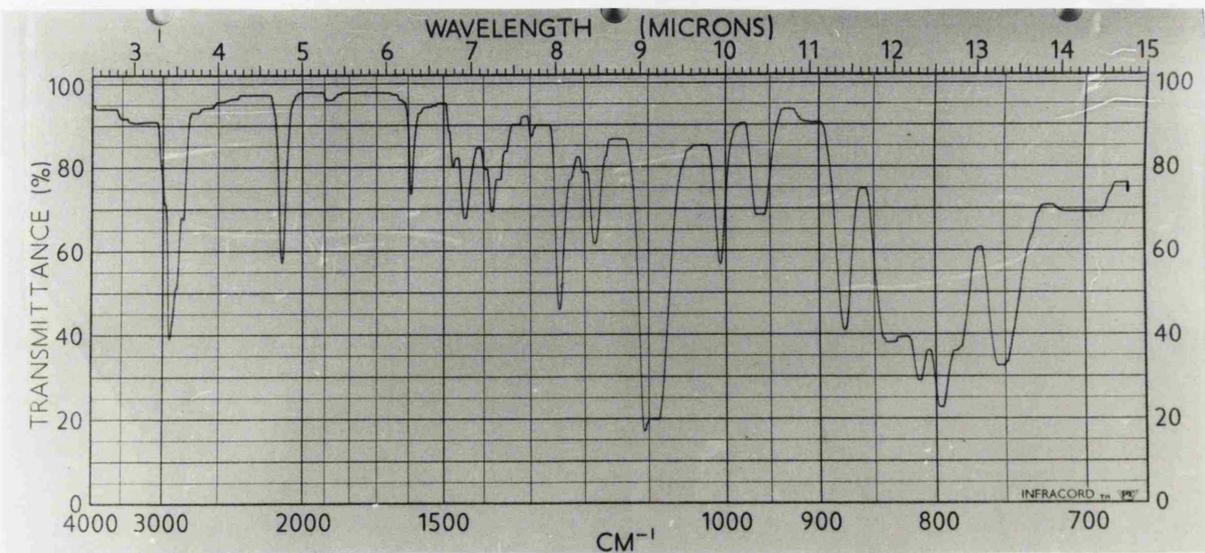
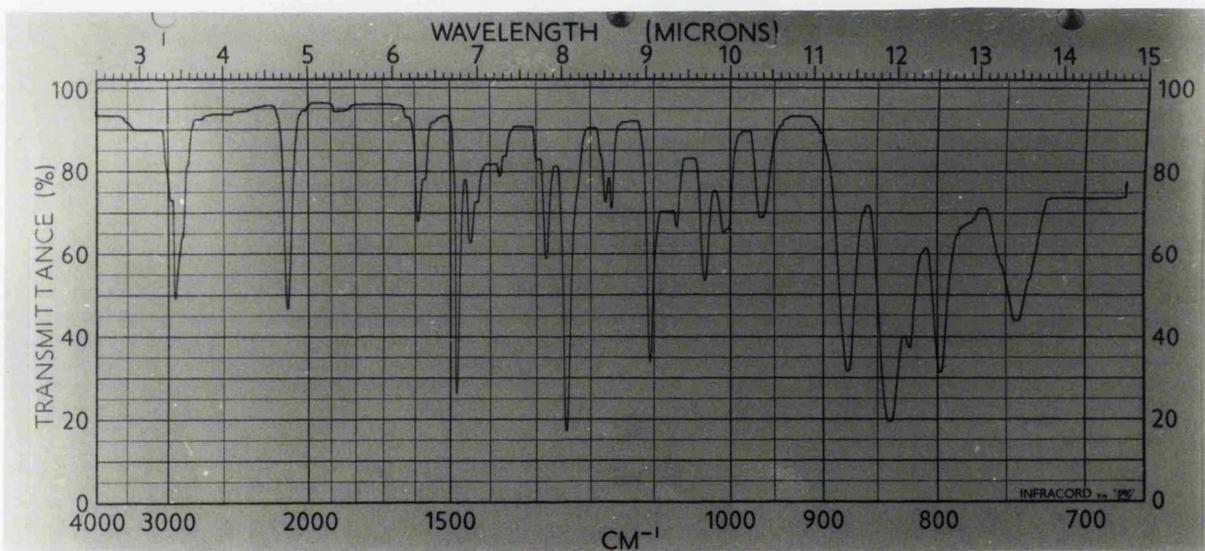
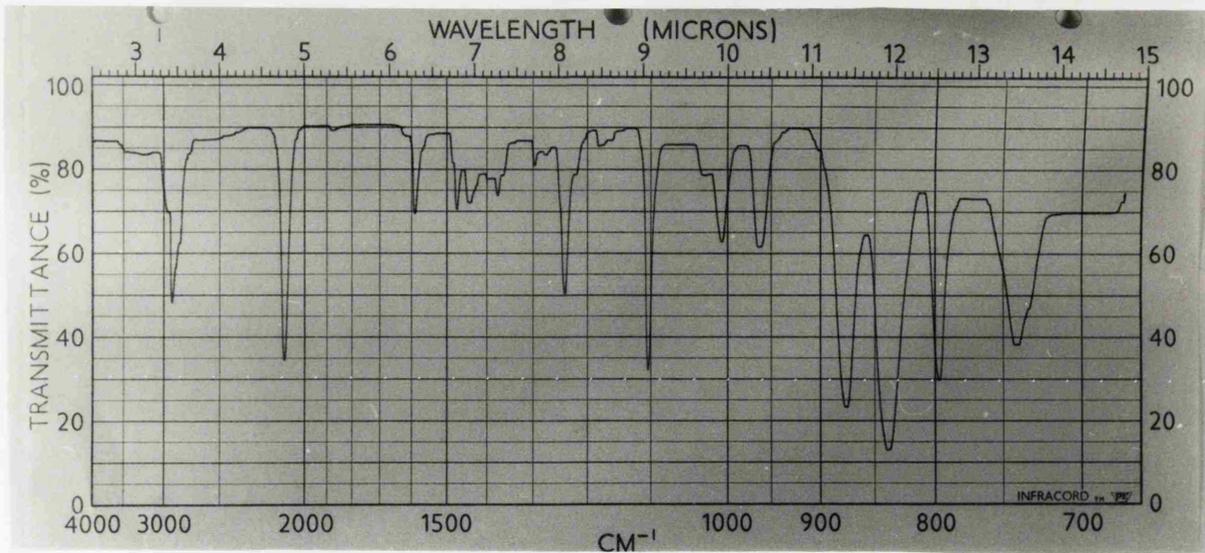
Fraction 2A, 0.90 g., " " " n_D^{25} 1.5373

Fraction 3A, 0.70 g., " " " n_D^{25} 1.5380

The three infrared spectra were apparently identical, showing the

presence of small amounts of OH and SiH. The Beilstein and Lassaigne tests showed halogen to be present in all fractions 1A, 2A, and 3A. The addition of an acidified solution of silver nitrate to an alcoholic solution of a sample of fraction 3A produced the characteristic⁶¹ reaction of a Si - H bond: the solution became orange, the colour turning rapidly to dark brown and then black, and there were signs of evolution of hydrogen. Provided the mixture was sufficiently acidified (with nitric acid), the reaction mixture eventually became clear and colourless, showing there to be no hydrolysable halogen in fraction 3A. The latter was taken to be partially brominated sym.-diethyldimethyldi(α -methoxy-p-tolyl)disiloxane (see the Discussion), $[\alpha]_D + 0.89^\circ$ in benzene (c, 17.4). (Found for fraction 3A: C, 63.27; H, 8.19; Br, 8.36. $C_{22}H_{34}O_3Si_2$ requires C, 65.64; H, 8.51; Br, -- %.)

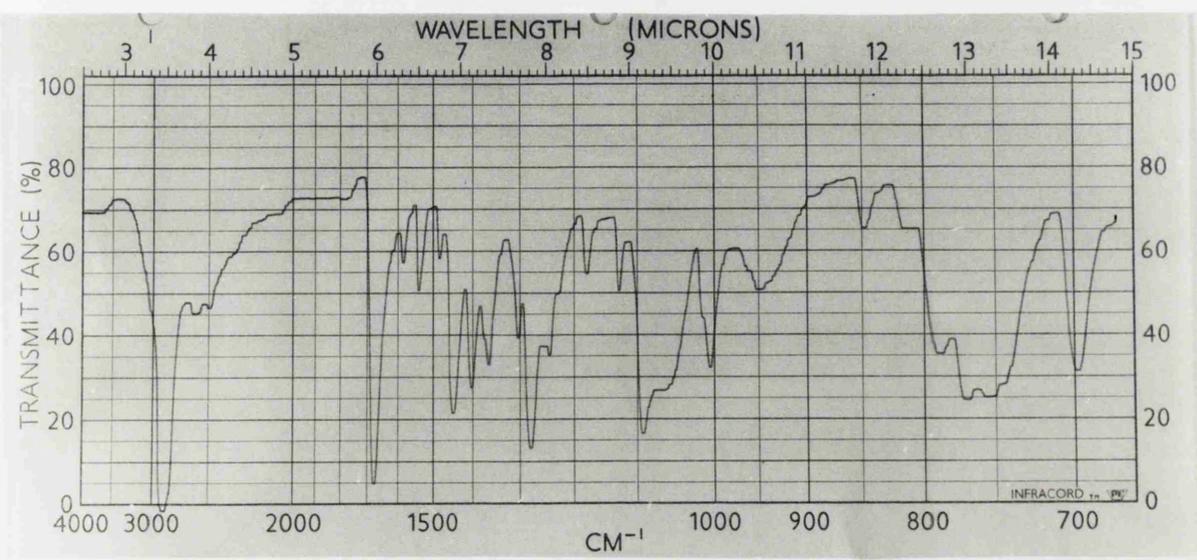
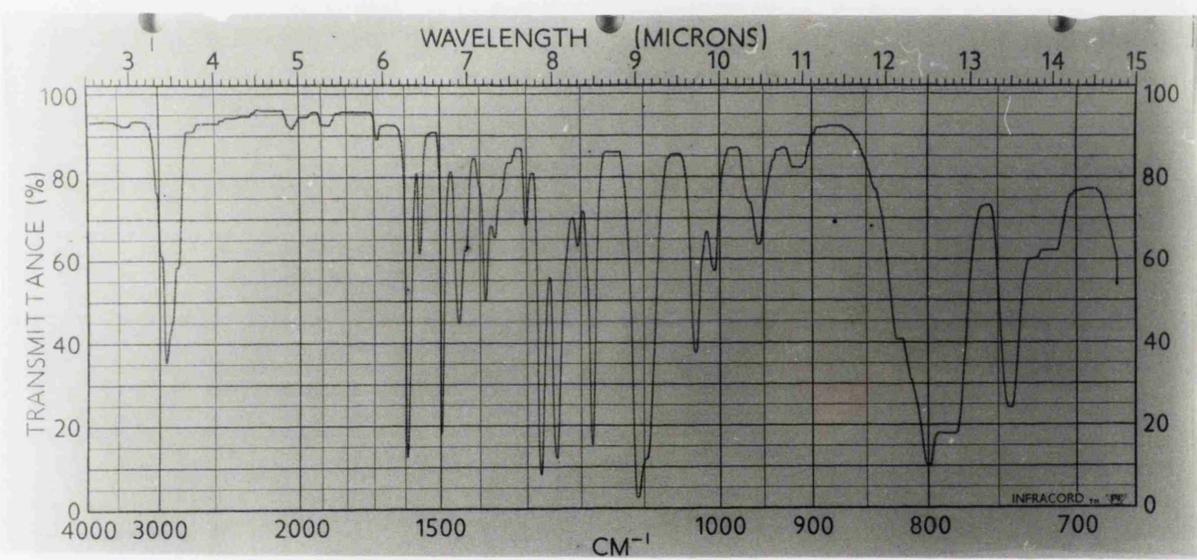
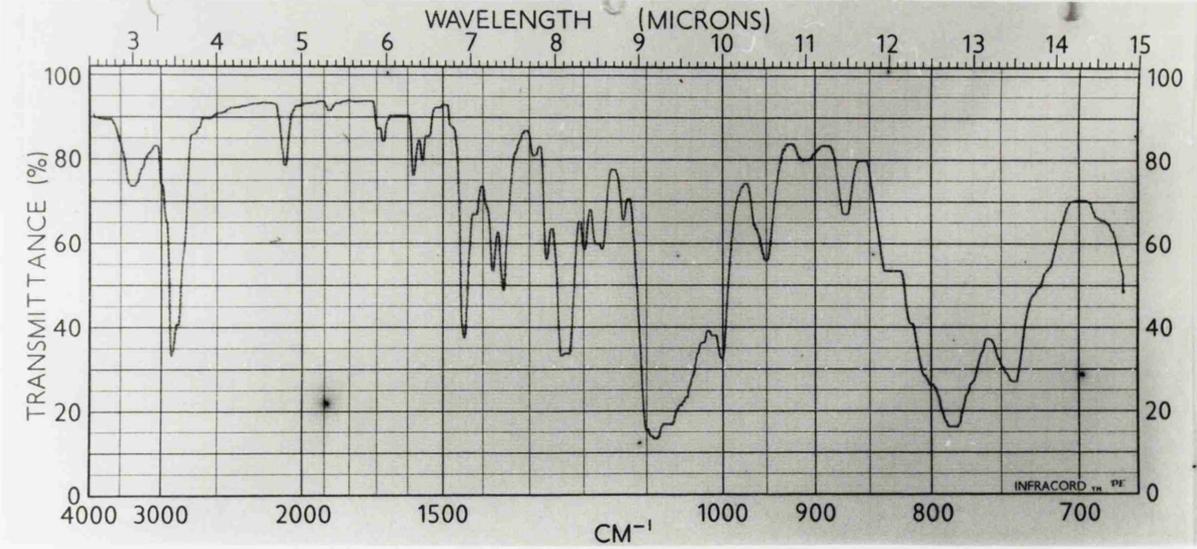
Fraction 2A (0.87 g.) was placed in a 0.5 dm. centre-filling polarimeter tube, and the minimum quantity (~ 4 ml.) of purified methanol was added. The observed rotation was $\alpha = + 0.10^\circ \pm 0.005$. The solution was removed, concentrated hydrochloric acid (0.3 ml.) added, and the homogeneous mixture refluxed for 3 hours. As much solvent as possible was distilled off at reduced pressure, and the residue freed from water and hydrogen chloride by standing it over potassium hydroxide pellets in an evacuated desiccator. The residue was washed into the same polarimeter tube as before, using the minimum of methanol (i.e., ~ 4 ml.): the observed rotation of the (now) rather yellow solution was $\alpha = + 0.09^\circ \pm 0.01$.



← The infrared spectrum of fraction 2A, p. 64

← The infrared spectrum of fraction 3A, p. 64

← The infrared spectrum of fraction 5A, p. 64



← The infrared spectrum of fraction 3A, p. 65

← The infrared spectrum of p-[ethylmethyl(p-methoxyphenyl)silyl]-
benzyl methyl ether, p. 54

← The infrared spectrum of sym-di(p-carboxyphenyl)diethyldimethyl-
disiloxane

PART TWO: The Methanolysis of Optically-Active Methylphenyl-
(α -naphthyl)methoxysilane

(A) The Preparation of the Optically-Active Tritium-Labelled
 Substrate

(i) Methylphenyldimethoxysilane.

Methylphenyldichlorosilane (956 g., 5.0 mole) [obtained from Midland Silicones] was added dropwise to a stirred slurry of magnesium methoxide in methanol, prepared by the reaction of magnesium turnings (121.6 g., 5.0 g. atoms) with methanol (1500 ml.).⁵⁵ The reaction mixture was refluxed for 7 hours, allowed to cool to room temperature overnight, then filtered to remove the crystalline solid. Petroleum spirit (b.p. 60-80°) (1500 ml.) was used to wash the magnesium salts. The filtrate was washed twice with ice-cold water, dried over anhydrous sodium sulphate, then fractionated to give the required compound, 590 g., 64.8 %, b.p. 204° / 753 mm., n_D^{25} 1.4782. Lit⁶³: b.p. 199-200°, n_D not given.

(ii) (+)-Methylphenyl(α -naphthyl)methoxysilane.²⁰

α -Bromonaphthalene

(621 g., 3.0 mole) was reacted with magnesium turnings (73.0 g., 3.0 g. atoms) in ether (200 ml.), under nitrogen, in a 3 litre 3-necked flask, in the normal way. After ~ 20 % addition of halide, tetrahydrofuran (100 ml.) and benzene (300 ml.) were added to retain homogeneity of the reaction mixture. After ~ 80 % addition of halide, tetrahydrofuran (100 ml.) and ether (200 ml.) were added for

the same reason. The mixture was stirred at room temperature for 2 hours, when some magnesium remained. To the red-brown solution, cooled in ice, was added rapidly methylphenyldimethoxysilane (546 g., 3.0 mole) which was washed in with tetrahydrofuran (50 ml.). On removing the cooling-bath, the reaction mixture became warm but no refluxing occurred. The mixture was refluxed for 20 hours, cooled, and hydrolysed by the slow addition of water (250 ml.) to give a clear orange solution plus coagulated solid. The solution was decanted off, and the residual solid washed similarly with ether (3 x 300 ml.). The combined ethereal solutions were washed with aqueous ammonium chloride solution (2 x 1000 ml.) then worked up as usual; removal of solvent gave a residue which was fractionated: the fore-run consisted of starting materials and naphthalene. The main fraction (578 g., 69 %) had b.p. 160° / $\frac{1}{2}$ -1 mm., and solidified almost immediately. A hasty measurement of the refractive index gave n_D^{25} 1.6133. Recrystallisation from hexane (450 ml.) gave 498 g. of product, m.p. $60.5-62.5^{\circ}$. Lit²⁰: m.p. $62.5-63.5^{\circ}$, n_D^{25} 1.6144.

(iii) The preparation of the diastereoisomeric methylphenyl(α -naphthyl)((-)-menthoxy)silanes.²⁰

(-)-Menthol (156.0 g., 1.0 mole)

[Eastman Kodak] and (+)-methylphenyl(α -naphthyl)methoxysilane (278 g., 1.0 mole) (m.p. $60.5-62.5^{\circ}$) were dissolved in toluene (400 ml.) and potassium hydroxide (0.1 g.) added. The mixture was refluxed, and the methanol-toluene azeotrope fractionated off via a glass-

helices packed column (1.4 x 30 cm.). 3 ml. of distillate were obtained in 3 hours. A further 0.1 g. of potassium hydroxide was added, and the mixture refluxed to obtain more azeotrope. Refluxing for a total of 40 hours brought the total volume of azeotrope to ~ 25 ml. The cooled solution was diluted with petroleum spirit (b.p. below 40°) (200 ml.) and passed down a column of silica-gel (100-200 mesh) (2.5 x 25 cm.), which was eluted with toluene (40 ml.). Solvent was stripped off of the combined eluents, and the residue fractionated: the forerun contained menthol and the starting methoxide; the main fraction was a syrup, 143.4 g. (35.7 %), b.p. 180-220° / 0.01 mm.

(iv) The isolation of (-)-methylphenyl(α -naphthyl)((-)-menthoxy)-silane.²⁰

The above syrup was dissolved in petroleum spirit (b.p. below 40°) (250 ml.) and cooled in an alcohol-Drikold slush bath for 24 hours, when the supernatant liquor (A) was decanted off, and the remaining solid recrystallised normally (from the same solvent) to give a solid B, 33.1 g., m.p. 83.5-85.0°, $[\alpha]_D - 54.2^\circ$ in cyclohexane (c, 11.32). Lit²⁰: m.p. 82-84°, $[\alpha]_D - 53.9^\circ$ under the same conditions.

The mother liquors from B gave a second crop (C) which was recrystallised as before to give 16.0 g. product, m.p. 83.5-85.0°.

(v) (+)-Methylphenyl(α -naphthyl)silane.²⁰

Lithium aluminium hydride

(8.2 g., 0.22 mole) was refluxed with diethyl ether (100 ml.) for 30 minutes, in a 3-necked 1 litre flask fitted with stirrer, condenser, dropping funnel, and guard tubes. To the slurry was added rapidly a solution of (-)-methylphenyl(α -naphthyl)((-)-menthoxy)silane (69.9 g., 0.174 mole) in di-n-butyl ether (100 ml.). Diethyl ether was allowed to evaporate from the heated and stirred mixture, until the temperature of the slurry was 78°. The stirrer was stopped, and the mixture was refluxed for 18 hours. Acetone (60 ml.) was added dropwise with stirring and ice-cooling, over ~ 45 minutes. The slurry was poured onto a mixture of crushed ice (~ 500 g.) and concentrated hydrochloric acid (120 ml.), and the mixture shaken and extracted with diethyl ether (3 times). The combined ethereal solutions were washed with cold water (3 times) and dried over anhydrous sodium sulphate. Solvent was removed at reduced pressure, and the residue heated to 180° / 2 mm. to remove menthol. When cooled, the residue solidified, and it was recrystallised (4 times) from petroleum spirit (b.p. 60-80°) to give a solid A, 6.15 g., m.p. 62.5-63.5°, $[\alpha]_D^{20} + 32.1^\circ$ in cyclohexane (c, 4.01). Lit²⁰: the most optically-pure silane had m.p. 63.5-64.5°, $[\alpha]_D^{20} + 33.7^\circ$ in cyclohexane (c, 4.00).

The mother liquors from A yielded a further 23.0 g. of solid, m.p. 62.5-63.5°.

(vi) (-)-Methylphenyl(α -naphthyl)silane.²⁰

The mother liquors from the isolation of (-)-methylphenyl(α -naphthyl)((-)-menthoxy)silane

[(iv), p. 71] on evaporation gave a syrup (58.1 g., 0.145 mole) which was treated as in (v), with lithium aluminium hydride (6.8 g., 0.18 mole), etc. The weight of crude (-)-silane thus produced was 33.8 g. Recrystallisation from hexane gave 12.0 g. of product, m.p. 61.5-62.5°, $[\alpha]_D - 32.7^\circ$ in cyclohexane (c, 6.04). Lit²⁰: m.p. 61.5-62.5°, $[\alpha]_D - 32.8^\circ$ in cyclohexane (c, 6.07).

The mother liquors yielded another 4.9 g., m.p. 60.5-62.5°

(vii) (+)-Methylphenyl(α -naphthyl)methoxysilane.²⁰

(-)-Methylphenyl-

(α -naphthyl)silane (12.4 g., 0.05 mole) was placed in a 250 ml. R.B. flask, fitted with a bung carrying gas inlet and outlet tubes. The inlet tube was furnished with a sintered-glass dispersion tip, and the outlet with "sulphuric acid bubblers". Carbon tetrachloride (40 ml.) was added, and the solution cooled in ice while chlorine was bubbled in via a drying train consisting of sulphuric acid traps. The reaction was stopped immediately the solution became yellow-green in colour, and purified petroleum spirit (b.p. below 40°) ("pentane") (100 ml.) added. This solution was added rapidly, with swirling, to a 1 litre separatory funnel containing "pentane" (300 ml.), cyclohexylamine (20 ml.), and methanol (10 ml.). The mixture was swirled for a few seconds, then washed with ice-cold water (6 x 200 ml.). The organic layer was dried over anhydrous sodium sulphate for 1½ hours, and the solvent removed at reduced pressure to leave a residue (19.7 g.) that smelled of cyclohexylamine. This residue was diluted with "pentane", and the solution

allowed to stand in the refrigerator, to obtain a crystalline deposit (A) which was filtered off. The mother liquors yielded a second crop (B). The solids A (8.15 g.) and B (3.85 g.) were individually redissolved in petroleum spirit (b.p. below 40°) (150 ml.), and washed with water (3 x 100 ml.) to remove cyclohexylamine hydrochloride. The solutions were dried as before, and the solvent removed to leave 8.10 g., and 3.80 g., of product, respectively.

Solid A was recrystallised from "pentane", to give C, 5.6 g., m.p. 63.5-64.5°, $[\alpha]_D^{20} + 14.2^\circ$ in "pentane" (c, 4.60). Solid B was recrystallised similarly, from the mother liquors from C, to give D, 3.6 g., m.p. 63.5-64.5°. Solid C was that used for the kinetic measurements. Lit²⁰: m.p. 64.5-65°, $[\alpha]_D^{20} + 16.5^\circ$ in pentane (c, 4.86).

(viii) (-)-Methylphenyl(α -naphthyl)(*methoxy)silane.

(+)-Methylphenyl(α -naphthyl)silane (24.8 g., 0.10 mole) was treated as in (vii), above, but using tritio-methanol [see p. 39], to yield a residue (37.8 g.) of crude (-)-methoxysilane. Crystallisation gave a solid (A), a second crop (B), and a third crop (C). Solid A (12.45 g.) was dissolved in petroleum spirit (b.p. below 40°) and washed with water as in (vii), above. The solvent was removed and the residue was recrystallised twice from "pentane", to give D: 6.60 g., m.p. 63-63.5°, $[\alpha]_D^{20} - 13.2^\circ$ in "pentane" (c, 4.99). The solids B (9.40 g.), and C (1.0 g.), were combined and dissolved in petroleum spirit (b.p. below 40°), and washed as for A, above, to remove cyclohexylamine hydrochloride, then recrystallised from the mother liquors of D.

The solid (E) thus obtained (wt. 11.85 g.) was redissolved in petroleum spirit and rewashed to remove a suspension of the amine hydrochloride. Removal of the solvent, followed by two recrystallisations from "pentane", gave a solid F: 4.6 g., m.p. 63.0-63.5°.

Solids D and F were those used for the kinetic measurements.

(B) The Kinetics of Methanolysis of Optically-Active Tritium-Labelled Methylphenyl(α -naphthyl)methoxysilane

(i) Reagents and apparatus.

The substrates used were those described on pp. 73-4. To conserve material, some kinetic runs employed non-tritiated (+)-methylphenyl(α -naphthyl)methoxysilane to which had been added a small quantity of the tritiated (-)-enantiomer.

The benzoic acid and sodium acetate were A.R. grade, and were fused in silica crucibles immediately before use.³⁸

The solvent methanol was dried by the method of Lund and Bjerrum⁴⁶, then fractionated from the magnesium methoxide via a 40-plate Dixon-gauze column into a 2 litre flask fitted with a "drechsel-bottle head" with relevant taps, such that methanol could be removed by the application of nitrogen pressure.

The nitrogen was "white-spot" quality, and was passed through calcium chloride and soda-lime before use.

The reaction vessels were graduated flasks (generally 100 ml.) with polythene stoppers, and were cleaned

by the following procedure:- The flasks were filled with alcoholic potassium hydroxide solution for ~ 30 minutes, rinsed briefly with water, filled with chromic acid solution for ~ 30 minutes, rinsed again with water, then filled with boiling water for ~ 10 minutes (twice). The flasks were left for at least 10 hours, filled with deionised water, rinsed out with purified methanol, and dried in an oven at 150° for 5 hours. The flasks were allowed to cool in vacuo.

The polarimeter employed was a Hilger "Microptic" polarimeter, model M 413, graduated in 0.01° divisions.

The polarimeter tube employed was a 2 dm. end-filling micro-tube, capacity ~ 2.5 ml.

(ii) General procedure.

(-)-Methoxysilane or a mixture of (-)- and (+)-methoxysilane (0.4-0.5 g.) was weighed into a reaction vessel, and to the flask was added a known weight or volume (30-40 g.) of purified methanol. After dissolution (~ 10 minutes) the vessel was immersed in a thermostat at 24.97°, and the catalyst (if any) added after a further 20-30 minutes. For details of catalysts, see the appropriate section below.

The first sample (~ 3 ml.) was withdrawn and its rotation measured [in the 2 dm. tube (above)] some 30 minutes after the addition of the catalyst, when the latter consisted of a large volume of a methanolic solution. When the catalyst was added either as a small (~ 1 ml.) volume of a methanolic

solution or as a solid, the first sample was removed some 5 minutes after the addition of the catalyst. Further samples were removed at intervals, and their rotations measured. [Aliquots of either 1 ml. or 2 ml. were removed at intervals by Dr. R. Baker or Mr. R. Spillett, for the purpose of radiochemical measurements. These results are collected into a separate section, p. 81.]

(iii) Polarimetric results.

The kinetic results tabulated below give for each run the weight of (-)-methylphenyl(α -naphthyl)(*methoxy)-silane [= (-)-R₃SiOMe*] and (where employed) the weight of (+)-methylphenyl(α -naphthyl)methoxysilane [= (+)-R₃SiOMe], and also the weight or volume of the methanolic reaction mixture before addition of any catalyst.

The density of the reaction mixtures, for the calculation of molarities, was taken to be that of methanol at 25°, i.e., 0.7865 g. / ml.

Also listed are the rotations (R) of samples withdrawn at relative times T, and the calculated values of k_{inv} for the successive readings, using the expression

$$k_{inv} = \frac{2.303}{2t} \cdot \log_{10} R_0 / R$$

where R_0 = initial rotation, at time = 0; R = rotation at time = t.

Finally, the graphical value of k_{inv} is given.

N.B. For $k_{inv} > 100 \times 10^{-7} \text{ sec.}^{-1}$, the times given are those at which the readings were made, not the

times at which the samples were withdrawn.

(a) Neutral solution.

RUN I: 0.1999 g. (-)-R₃SiOMe*, in 25 ml. solution.

T (hrs.):	0	66.95	138.95	257.95	378.95
-R (deg.):	0.290	0.210	0.160	0.095	0.055
10 ⁷ k _{inv} (sec. ⁻¹):	-	6.68	5.95	6.01	6.09

Graphically, k_{inv} = 6.1 x 10⁻⁷ sec.⁻¹

(Radiochemical measurements were not made for run 1)

RUN II: 0.0608 g. (-)-R₃SiOMe*; 0.4495 g. (+)-R₃SiOMe, in 47.2 g. solution.

T (hrs.):	0	68.00	137.00	213.00	268.00	318.00	381.00
+R (deg.):	0.250	0.190	0.135	0.100	0.080	0.065	0.050
10 ⁷ k _{inv} (sec. ⁻¹):	-	5.60	6.25	5.97	5.91	5.88	5.87

Graphically, k_{inv} = 5.9 x 10⁻⁷ sec.⁻¹

RUN III: 0.0568 g. (-)-R₃SiOMe*; 0.4785 g. (+)-R₃SiOMe, in 50 ml. solution.

T (hrs.):	0	46.00	112.40	187.60	268.20
+R (deg.):	0.340	0.275	0.190	0.130	0.085
10 ⁷ k _{inv} (sec. ⁻¹):	-	6.40	7.20	7.12	7.18

Graphically, k_{inv} = 7.2 x 10⁻⁷ sec.⁻¹

(b) Sodium acetate solution.

A solution of 0.0444 g. sodium acetate in 147.3 g. methanol was prepared, i.e., molarity = 2.90 x 10⁻³ M in sodium acetate.

RUN IV: 0.0619 g. (-)-R₃SiOMe*; 0.5315 g. (+)-R₃SiOMe, in 25 ml.

solution. To the solution was added 25 ml. of the above sodium acetate solution, i.e., the reaction mixture was 1.45×10^{-3} M in sodium acetate.

T (hrs.):	0	3.00	8.00	13.00	24.00	30.00	36.00
+R (deg.):	0.330	0.285	0.230	0.180	0.105	0.080	0.050
$10^7 k_{inv}$ (sec. ⁻¹):	-	67.9	62.7	64.8	66.3	65.6	72.8

Graphically, $k_{inv} = 66.0 \times 10^{-7}$ sec.⁻¹

RUN V: 0.0603 g. (-)-R₃SiOMe*; 0.5006 g. (+)-R₃SiOMe, in 25 ml. solution. To the solution was added 25 ml. of the above sodium acetate solution as for run IV, i.e., the reaction mixture was 1.45×10^{-3} M in sodium acetate.

T (hrs.):	0	3.50	8.00	13.00	23.00	29.00
+R (deg.):	0.305	0.255	0.195	0.150	0.080	0.055
$10^7 k_{inv}$ (sec. ⁻¹):	-	71.1	77.7	75.8	80.8	82.0

Graphically, $k_{inv} = 80.0 \times 10^{-7}$ sec.⁻¹

RUN VI: 0.5291 g. (-)-R₃SiOMe*, in 34.05 g. solution. To the solution was added 0.0040 g. sodium acetate, i.e., the reaction mixture was 1.13×10^{-3} M in sodium acetate.

T (hrs.):	0	3.25	6.60	8.75	11.55	22.70	26.25
-R (deg.):	0.480	0.360	0.290	0.260	0.220	0.120	0.095
$10^7 k_{inv}$ (sec. ⁻¹):	-	122.9	106.2	97.3	93.8	84.8	85.7

T:	29.25	33.40
-R:	0.080	0.060
$10^7 k_{inv}$:	85.1	86.5

$$\text{Graphically, } k_{\text{inv}} = 85.2 \times 10^{-7} \text{ sec.}^{-1}$$

(c) Sodium methoxide solution.

A solution of 0.0046 g. sodium metal in 80.0 g. methanol was prepared, i.e., molarity = 1.97×10^{-3} M in sodium methoxide.

RUN VII: 0.4243 g. (-)-R₃SiOMe*, in 35.65 g. solution. To the solution was added 1.0 ml. of the above sodium methoxide solution, i.e., the reaction mixture was 4.25×10^{-5} M in sodium methoxide. An atmosphere of nitrogen was maintained above the reaction mixture.

T (min.):	0	19	46	81	136	185
-R (deg.):	0.350	0.290	0.230	0.165	0.100	0.070
$10^7 k_{\text{inv}}$ (sec. ⁻¹):	-	824	761	774	768	725

RUN VIII: 0.4195 g. (-)-R₃SiOMe*, in 38.05 g. solution. To the solution was added 1.0 ml. of the above sodium methoxide solution, i.e., the reaction mixture was 4.0×10^{-5} M in sodium methoxide.

An atmosphere of nitrogen was maintained above the reaction mixture.

T (min.):	0	32	83	157	228	339	565
-R (deg.):	0.370	0.300	0.230	0.170	0.130	0.105	0.055
$10^7 k_{\text{inv}}$ (sec. ⁻¹):	-	545	478	413	382	310	281

RUN IX: 0.4175 g. (-)-R₃SiOMe*, in 36.15 g. solution. To the solution was added 1.5 ml. of the above sodium methoxide solution, i.e., the reaction mixture was 6.2×10^{-5} M in sodium methoxide. An atmosphere of nitrogen was maintained above the reaction mixture.

T (min.):	0	23	42	63	90
-R (deg.):	0.320	0.205	0.125	0.085	0.055

$10^7 k_{inv}$ (sec.⁻¹): - 1616 1866 1754 1632

(d) Benzoic acid solution.

No stock solution of the catalyst was prepared.

RUN X: 0.3826 g. (-)-R₃SiOMe*, in 29.05 g. solution. To the solution was added 0.0050 g. benzoic acid, i.e., the reaction mixture was 1.1×10^{-3} M in benzoic acid.

T (min.):	0	15	33	55	84	117	172
-R (deg.):	0.430	0.350	0.280	0.210	0.150	0.110	0.055
$10^7 k_{inv}$ (sec. ⁻¹):	-	1141	1084	1085	1045	972	996

Graphically, $k_{inv} = 1016 \times 10^{-7}$ sec.⁻¹

RUN XI: 0.4431 g. (-)-R₃SiOMe*, in 35.20 g. solution. To the solution was added 0.0052 g. benzoic acid, i.e., the reaction mixture was 0.95×10^{-3} M in benzoic acid.

T (min.):	0	13	36	56	81	126	166
-R (deg.):	0.410	0.360	0.270	0.220	0.170	0.115	0.075
$10^7 k_{inv}$ (sec. ⁻¹):	-	834	966	926	907	841	853

Graphically, $k_{inv} = 878 \times 10^{-7}$ sec.⁻¹

(iv) Radiochemical results.

The work detailed in this section was performed by Dr. R. Baker and Mr. R. Spillet. The method was essentially that developed by Martin.³⁸

Aliquots of 2 ml. or 1 ml. (according to the concentration of tritium-labelled substrate in the reaction mixture) were removed at intervals from the solutions described

in section (iii) [pp. 77-81], and added to 20 ml. scintillator solution. Immediately, 150 ml. of aqueous ammonium chloride solution (5 g. / litre) were added, and the toluene layer separated after shaking the mixture thoroughly. The toluene solution was washed with water (3 times), and dried over sodium sulphate. Aliquots (10 ml. or 20 ml., according to the concentration of the tritium-labelled substrate in the reaction mixture) were pipetted into the counting cell, and the radioactivity measured.⁵⁶

Except for rapid (k_{tot} greater than $100 \times 10^{-7} \text{ sec.}^{-1}$) runs, the toluene solutions were not "counted" immediately but retained until all solutions could be counted within 6 hours.

For each run are listed the net galvanometer deflections (D) observed for aliquots withdrawn at relative times T. Also given is the graphical value of k_{tot} , the pseudo-first order rate constant for the methanolysis reaction.

RUN II: 2 ml. of the reaction mixture; 20 ml. of the toluene solution for counting.

T (hrs.):	0	211.2	282.9	378	456	552
D (mm.):	110.1	71.2	61.1	48.6	39.1	33.5

$$\text{Graphically, } k_{\text{tot}} = 6.64 \times 10^{-7} \text{ sec.}^{-1}$$

RUN III: Volumes as for run II.

T (hrs.):	0	91.0	169.0	265.5	331.0
D (mm.):	123.0	94.6	77.2	64.0	53.2

$$\text{Graphically, } k_{\text{tot}} = 7.06 \times 10^{-7} \text{ sec.}^{-1}$$

RUN IV: Volumes as for run II.

T (hrs.):	0	5.05	11.0	23.65	32.35	47.65
D (mm.):	124.7	105.7	93.2	70.1	57.4	42.8

$$\text{Graphically, } k_{\text{tot}} = 64.5 \times 10^{-7} \text{ sec.}^{-1}$$

RUN V: Volumes as for run II.

T (hrs.):	0	5.2	10.6	23.2	31.95	47.2
D (mm.):	116.2	99.2	84.2	58.9	46.5	32.0

$$\text{Graphically, } k_{\text{tot}} = 82.9 \times 10^{-7} \text{ sec.}^{-1}$$

RUN VI: 1 ml. of the reaction mixture; 10 ml. of the toluene solution for counting.

T (hrs.):	0	5.85	11.45	23.35	31.75	47.15
D (mm.):	463.2	369.8	314.5	220.2	171.7	114.3

$$\text{Graphically, } k_{\text{tot}} = 84.6 \times 10^{-7} \text{ sec.}^{-1}$$

RUN VII: Volumes as for run VI.

T (min.):	0	18	54	126	210	300
D (mm.):	187.5	163.5	134.5	98.5	75.5	61.5

RUN VIII: Volumes as for run VI.

T (min.):	0	43	104	189	258	337	567
D (mm.):	186.6	166.0	146.5	123.5	115.9	100.5	81.3

RUN IX: Volumes as for run VI.

T (min.):	0	20	40	60	84	157	304
D (mm.):	174.5	136.6	110.5	89.1	70.3	40.7	17.5

RUN X: Volumes as for run VI.

T (hrs.):	0	0.4	0.8	1.5	2.4	3.5
D (mm.):	480.8	416.1	357.3	282.0	204.4	138.9

Graphically, $k_{\text{tot}} = 1010 \times 10^{-7} \text{ sec.}^{-1}$

RUN XI: Volumes as for run VI.

T (hrs.):	0	0.4	0.8	1.5	2.5	3.5
D (mm.):	472.4	429.5	380.7	304.6	209.7	156.6

Graphically, $k_{\text{tot}} = 900 \times 10^{-7} \text{ sec.}^{-1}$

DISCUSSIONGeneral

As was pointed out on p. 25, the work of Hughes et al.³⁴ on symmetrical exchange reactions involving isotope-labelled nucleophiles was of great importance in showing that, within experimental error, nucleophilic substitution at saturated carbon occurs always with inversion of configuration. In the same way, the investigation of similar reactions involving asymmetric organosilicon compounds should show the relative extent of "flank attack" to "rear attack", or more precisely, "retentive attack" to "invertive attack". The latter distinction is necessary because the original hypothesis of Sommer and Bennett (p. 20), postulating⁶ angles of attack by the nucleophile of either 180° or 90° to the Si - leaving-group bond, failed to include the possibility of the attack being at 120° to this bond.³⁰ The stereochemical implications of the various angles of attack are analysed more fully in PART THREE of this Discussion (below), but for much of this Discussion the terms "invertive" and "retentive" will be used, referring to the observed result instead of to the (supposed) mechanism.

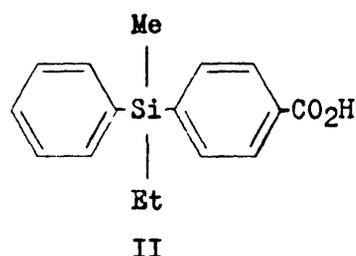
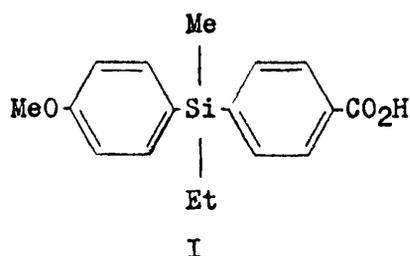
The aim of the work presented in this Thesis was the preparation of an optically-active alkoxysilane labelled with tritium in the alkoxy group, in order to compare its total exchange rate in the appropriate alcohol with (under the same conditions) its invertive exchange rate (loosely, the rate of racemisation). Although the intended substrate (arylethylmethylisopropoxysilane) could not

be obtained optically-active, the tritium-labelled analogue of methylphenyl(α -naphthyl)methoxysilane was readily prepared according to the method of Sommer and Frye (see p. 11), and was used instead for the kinetic measurements. The latter preparation, together with the kinetic measurements, is considered separately in PART TWO of this Discussion.

PART ONE: The Preparation of Optically-Active Compounds Containing the Arylethylmethylsilyl Group.

(A) Optically-Active p-[Ethylmethyl(p-methoxyphenyl)silyl]benzoic Acid

Following on the work of Pitt,^{28,29} the starting point for the preparation of the optically-active organosilicon compounds described herein was p-[ethylmethyl(p-methoxyphenyl)silyl]benzoic acid (I).

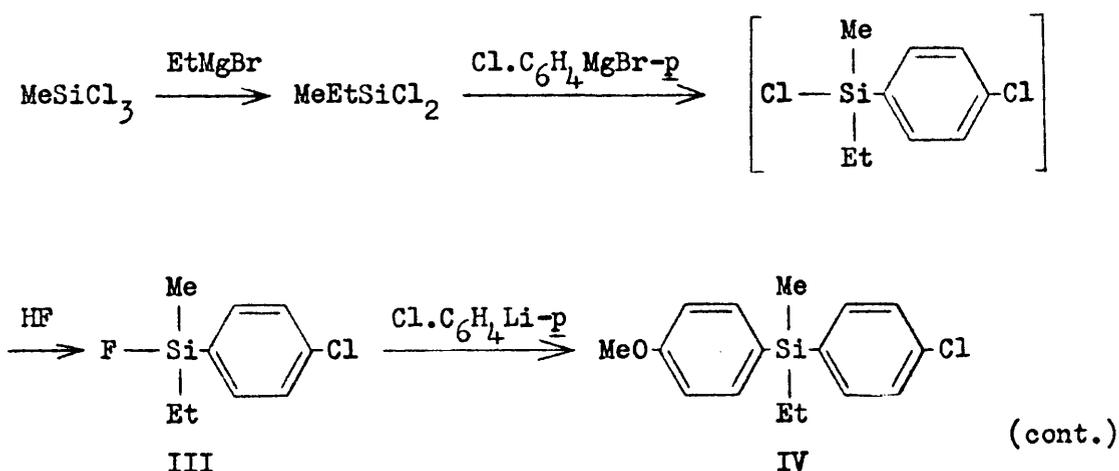


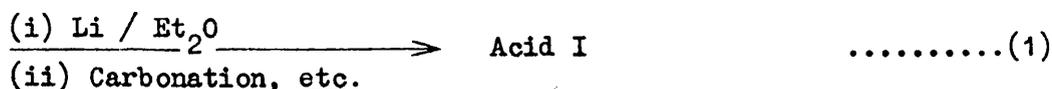
$[\alpha]_D +1.2^\circ$ in benzene (c , 3.68). $[\alpha]_D +2.8^\circ$ in benzene (c , 2.82).
This acid (I) differs from that (II) prepared and resolved by Pitt (see p. 7) by virtue only of a methoxy group, intended to increase the rate of halogen cleavage of the relevant Si - C bond, thereby eliminating, it was hoped, side reactions of the halogen with, for example, the ethyl group. Although the ethyl group is far from

ideal, being very similar to the methyl, it was retained because it was thought less likely to react with halogen than would, for example, isopropyl, and because it was hoped that the acid I would be amenable to resolution under the same conditions as were successful for the acid II. This hope was in fact realised.

Despite the acids I and II being very similar, the high reactivity of the Si - C₆H₄OMe-p bond towards (inter alia) mineral acid did not allow an analogous method of preparation. The acid II was prepared by oxidation of the corresponding p-tolyl compound, which was prepared from ethylmethylphenylfluorosilane, and the latter was prepared by heating the silanol with aqueous-alcoholic hydrofluoric acid solution at 60° for several hours. An equivalent preparation of the acid I would require the subjection of a p-methoxyphenyl - Si, or at best a p-tolyl - Si, bond to the latter process, and therefore this route was not attempted.

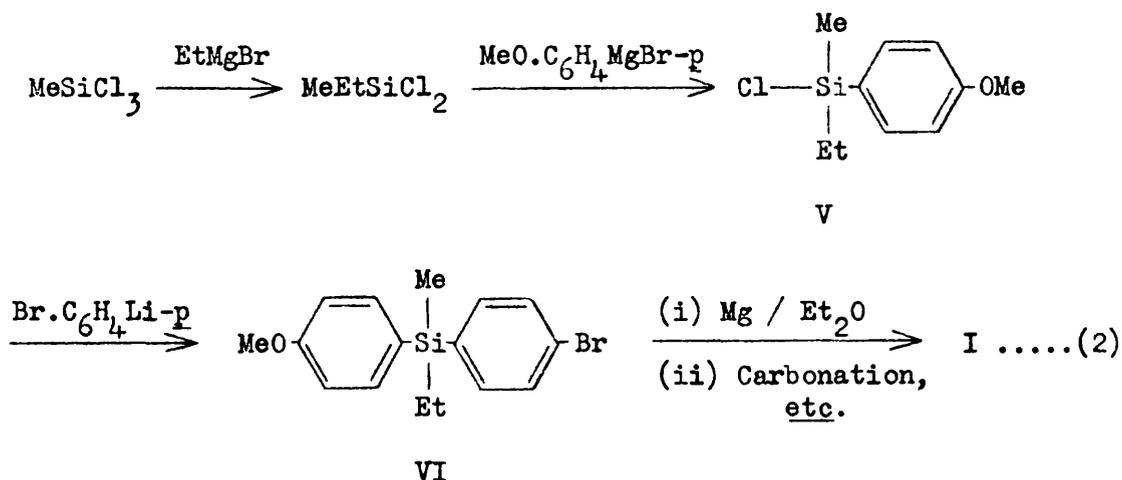
The first route to the acid I to be tried was the following (reaction scheme 1):





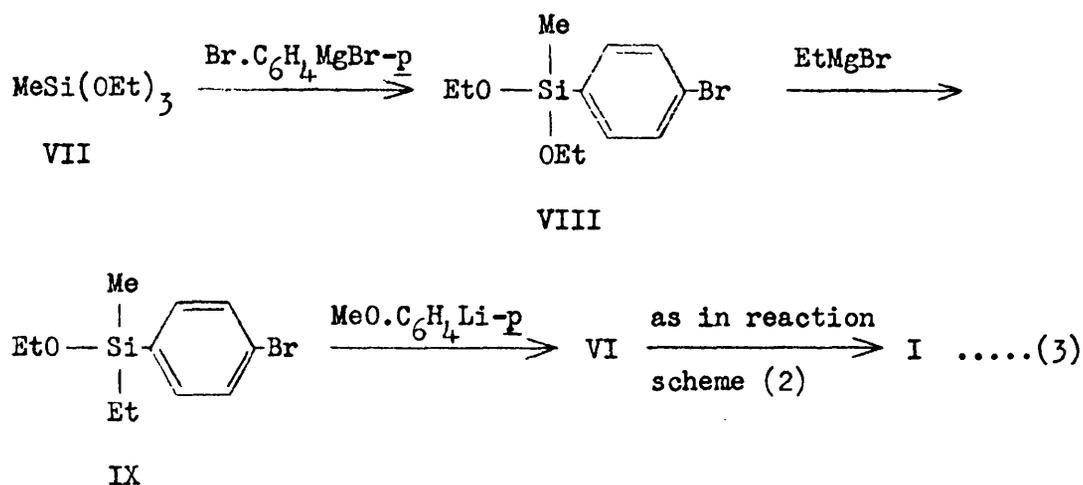
p-Chlorophenylethylmethylfluorosilane (III) was prepared successfully, as was p-chlorophenylethylmethyl(p-methoxyphenyl)silane (IV), although the carbon and hydrogen analysis of the latter was not satisfactory, probably due to p-dianisyl or a related substance (arising from the preparation of p-methoxyphenyl-lithium) subliming along with the required compound IV. The reaction of IV with lithium proceeded with difficulty, and carbonation of the reaction mixture gave a very poor yield of an acidic material which could not be crystallised (p. 46). The bulk of the starting material (IV) was recovered unchanged.

Accordingly, a second route to the preparation of the acid was attempted (reaction scheme 2):



This scheme was successful, but the overall yield of the acid (I) was so poor (2.2 %, based on the methyltrichlorosilane) that a modified route (reaction scheme 3) was used for the subsequent prepar-

ations of the acid:



Methyltriethoxysilane (VII) was chosen as the starting material only because it was readily available; the trimethoxysilane would have been more suitable since compounds VIII and IX have very similar boiling points. In practice, however, no difficulty was encountered, presumably because of the large difference in reactivity between the ethoxy groups of compound VIII.

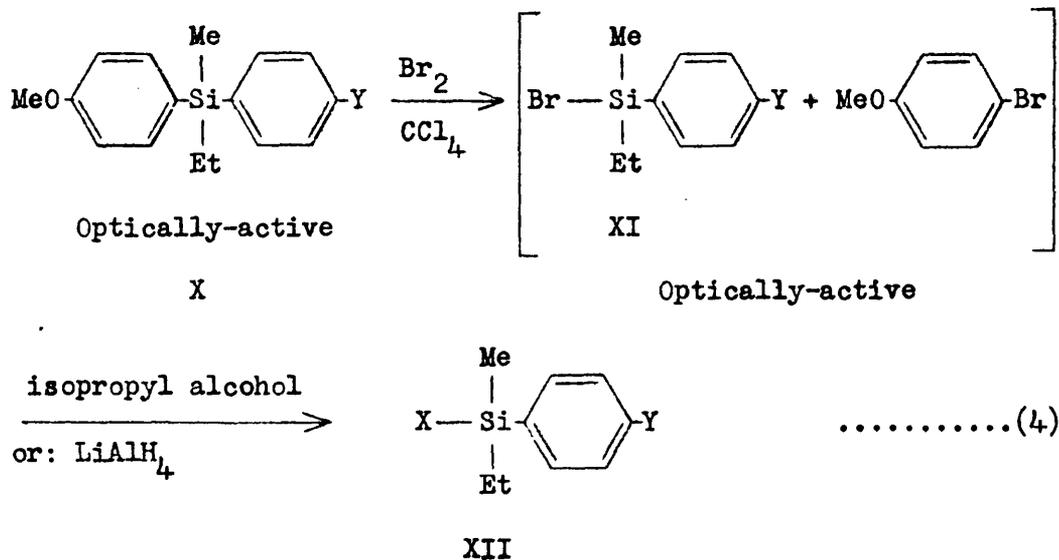
The overall yield of *p*-bromophenylethylmethylethoxysilane (IX) by this scheme was 33 %, but this value was considerably increased (to 66 %) when the intermediate *p*-bromophenylmethyldiethoxysilane (VIII) was not isolated.

Resolution of (+)-*p*-[ethylmethyl(*p*-methoxyphenyl)silyl]benzoic acid (I) was effected by means of its (-)-quinine salt, following the method found to be effective²⁹ for the resolution of (+)-*p*-(ethylmethylphenylsilyl)benzoic acid (II). The melting point of the optically-active acid I was found to be identical with that

of the racemic acid. The specific rotation of the acid I was even smaller than that of the acid II (see p. 86), but was still of opposite sign to that of the resolving agent.

(B) Derivatives of Optically-Active p-[Ethylmethyl(p-methoxyphenyl)silyl]benzoic Acid

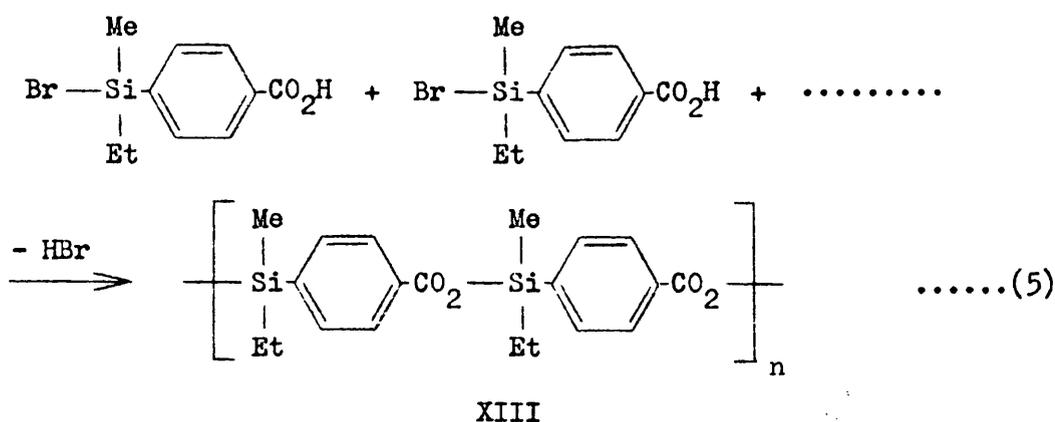
The following general reaction scheme (4) was employed for the attempted preparation of optically-active silicon-functional compounds:



where Y = CO₂H; CO₂Me; CH₂OMe;
and X = H; OPrⁱ;

Initially, it was hoped that the carboxyl group of the parent acid (I) could be retained (X: Y = CO₂H), because this group would be likely to confer crystallinity upon the required isopropoxysilane (XII: Y = CO₂H, X = OPrⁱ), although it was realised that the intermediate bromosilane (XI: Y = CO₂H) could eliminate hydrogen bromide

to form a polymeric acyloxysilane:^{57a}

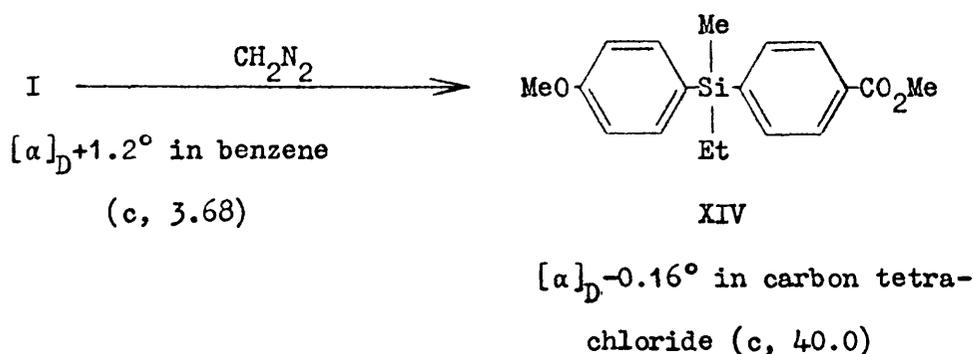


The isopropoxy group was chosen for X throughout these preparations where an alkoxy group was required, because it was thought that a methoxy (or ethoxy) group in an arylolethylmethylalkoxysilane would be much too reactive for the purpose of the proposed kinetic investigations.

Soon after these cleavage experiments (reaction scheme 4) were begun, Sommer and Frye published the outline of their preparation of optically-active methylphenyl(α -naphthyl)methoxysilane from the corresponding optically-active chlorosilane, employing methanol in pentane as solvent, with cyclohexylamine as the hydrogen chloride acceptor.¹³ It was therefore decided to apply this proven method as closely as practicable to the isopropanolysis of arylolethylmethylbromosilanes (XI) prepared as in reaction scheme 4 (p. 90).

Treatment in this fashion of the solution obtained from the bromine cleavage of acid I gave some disiloxane (as obtained by Pitt: see p. 8), but mainly a solid of high and indeterminate

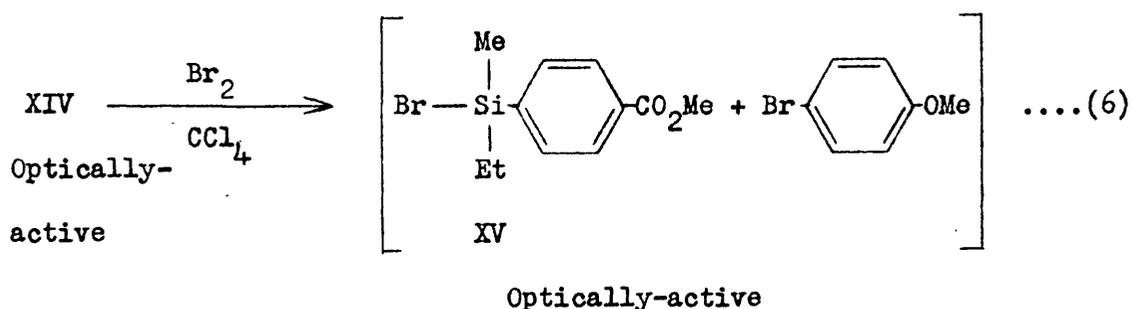
melting point, which was probably the polymeric acyloxysilane XIII. In order to prevent such acyloxysilane formation, an (unsuccessful) attempt was made to eliminate the carboxyl group from the acid I: when the acid I was heated with soda-lime in the usual way, cleavage of the p-methoxyphenyl - Si bond occurred, while other conventional methods of decarboxylation involve strongly acid conditions which would certainly cause disruption of this bond. The alternative was to block the functional group by esterification:



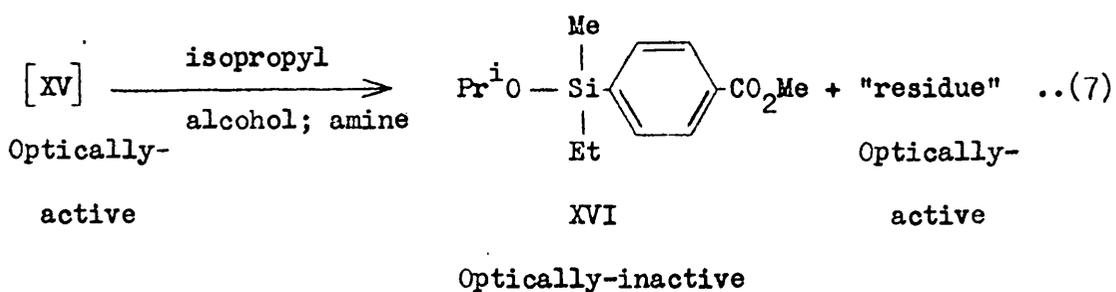
Unfortunately, the resulting methyl p-[ethylmethyl(p-methoxyphenyl)-silyl]benzoate (XIV) had an extremely small specific rotation.

Bromine cleavage of the optically-active ester XIV in carbon tetrachloride solution, in a polarimeter tube, changed the sign of optical rotation of the solution, and, more important, increased the rotation from -0.02° to $+0.08^\circ$. Over a period of 7 hours at room temperature the rotation dropped to $+0.02^\circ$. It was inferred that this was the result of the formation of the required optically-active bromosilane XV (reaction scheme 6, p. 93), followed by quite rapid racemisation due, perhaps, to the presence of bromide ion.^{39,40} However, no attempt was made at isolating the bromosilane XV when

the bromine cleavage was repeated on a preparative scale, because of the probable optical instability of the bromosilane on distillation.



Instead, the reaction mixture from reaction 6 was treated with isopropyl alcohol and cyclohexylamine in purified petroleum spirit (b.p. 60-80°) to obtain the corresponding isopropoxysilane XVI (reaction scheme 7), which was optically-inactive:



The residue from the fractionation of the isopropoxysilane XVI was, however, optically-active (much more so than the same amount of the starting material (XIV)), and accounted for all the activity of the reaction mixture prior to distillation. That is, some optically active by-product was formed in reaction 6 or 7, presumably a halogen-derivative of the starting material (XIV). Nevertheless, the optical-activity of this unknown substance was not sufficient to

account for the large (initial) increase in rotation observed for reaction 6, or for the subsequently observed fall in rotation.

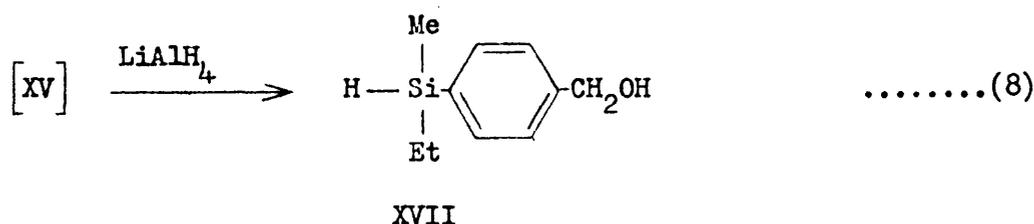
The lack of optical-activity of the isopropoxysilane XVI might have been due to one, or a combination, of several possible causes:

- (a) The bromine cleavage of the optically-active ester XIV (reaction 6) was not stereospecific. The only evidence of such stereospecificity is the observation of greatly increased rotation and subsequent (partial) racemisation, on carrying out the reaction in a polarimeter tube. The residual, time-independent, optical activity can be attributed to the unknown by-product that caused the reaction mixture from reaction 7 to be optically-active.
- (b) The isopropanolysis of the bromosilane XV (reaction 7) was not stereospecific, although the conditions were chosen to duplicate, as far as possible, those employed²⁰ by Sommer and Frye for the stereospecific methanolysis of optically-active methylphenyl-(α -naphthyl)chlorosilane. Such a lack of stereospecificity would be at variance with the deduction of Sommer and Frye that all reactions of acyclic chloro- (and bromo-) silanes occur with predominant inversion of configuration because of the ease with which chloro- and bromo- groups are displaceable from silicon³⁰ (see p. 32).
- (c) The isopropoxysilane XVI was not optically stable, the compound racemising before its rotation could be measured. Now the isopropoxysilane XVI was found to be quite sensitive to moisture,

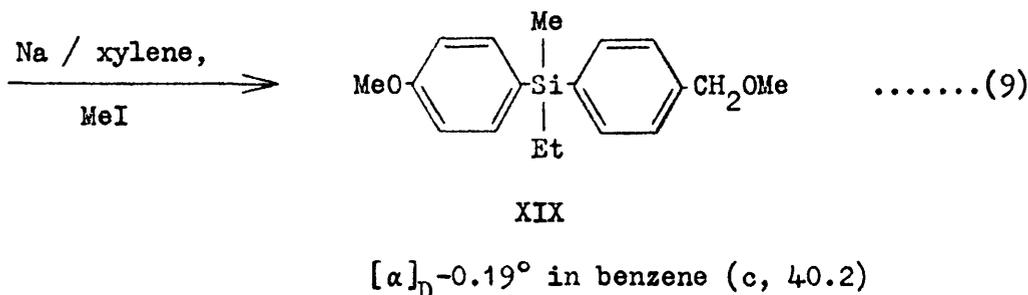
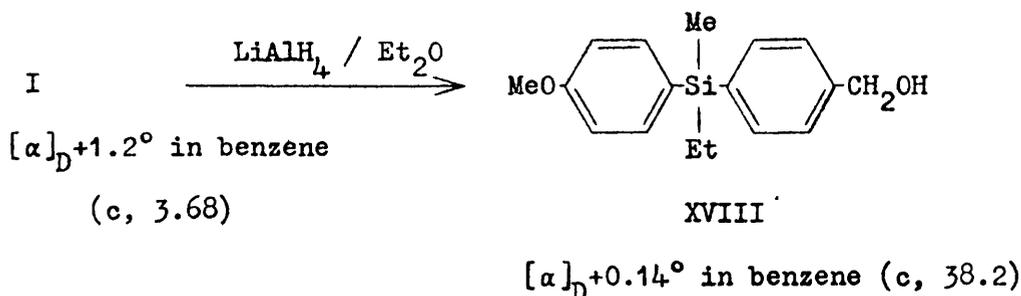
by contrast with methylphenyl(α -naphthyl)methoxysilane. Consequently, it is reasonable to postulate that the required optically-active isopropoxysilane XVI (if ever present) racemised very rapidly in the presence of excess isopropanol and much amine hydrobromide (a catalyst) before the alcohol, etc., could be extracted with water (or even while the reaction solution was being concentrated: cyclohexylamine and cyclohexylamine hydrobromide were present in the final, concentrated, solution; it is therefore possible that isopropyl alcohol was retained also, see p. 108.), although the method was successful for the preparation of optically-active methylphenyl(α -naphthyl)methoxysilane. To ensure that no mistake was being made in the application, to this isopropanolysis, of the technique of Sommer and Frye, the process was repeated using the compounds employed by those workers: the optically-active methylphenyl(α -naphthyl)methoxysilane was readily obtained, and was later put to the use for which the isopropoxysilane XVI had been required (PART TWO of this Discussion, p. 104).

It was decided therefore to attempt the reduction, by means of lithium aluminium hydride, of the apparently optically-active bromosilane XV since it seemed likely (from consideration of the work of Sommer and Frye,³⁰ and also of the strength of the Si - H bond) that the reaction would be stereospecific and the Si - H bond would be optically stable once formed (reaction scheme 4: Y = CO₂Me, X = H). However, it was necessary first to convert the carbometh-

oxy group to a non-reducible group, to avoid the preparation (as in reaction scheme 8) of the corresponding substituted benzyl alcohol XVII which would be useless as an intermediate should it be obtained optically-active:



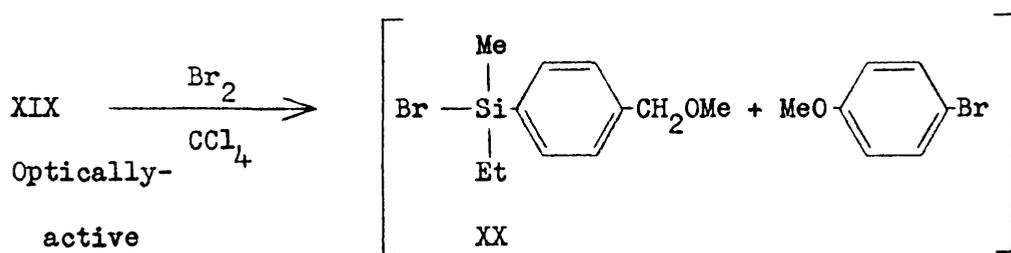
The scheme envisaged proceeded as follows (reaction scheme 9):



p-[Ethylmethyl(p-methoxyphenyl)silyl]benzyl alcohol (XVIII), and p-[ethylmethyl(p-methoxyphenyl)silyl]benzyl methyl ether (XIX), were prepared by essentially standard procedures from the optically-active parent acid I, and were of course optically-active although (like the corresponding methyl ester XIV) their specific rotations

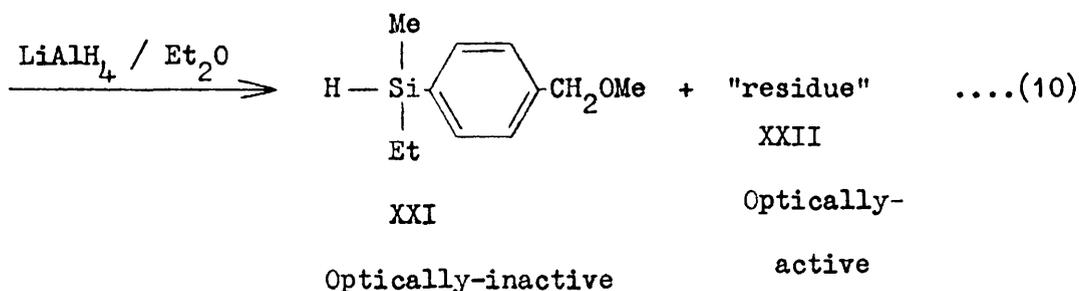
were substantially less than that of *p*-[ethylmethyl(*p*-methoxyphenyl)silyl]benzoic acid (I).

The methyl ether XIX was subjected in a polarimeter tube to bromination in carbon tetrachloride solution, as in reaction 6. By contrast with the bromine cleavage of (-)-methyl *p*-[ethylmethyl(*p*-methoxyphenyl)silyl]benzoate (XIV), the result was not a large increase of rotation; instead the rotation changed from -0.02° to $+0.02^\circ$, the latter value remaining constant over 6 days. Evidently an optically-active compound had been produced in the bromination reaction, but its rotation was strongly reminiscent of the unknown optically-active by-product from the bromination of the (-)-methyl ester (XIV). Further, it seemed that the required bromosilane XX (below) either was not optically-active when formed or was very unstable optically, since the constant value of the rotation given above ($+0.02^\circ$) was observed within 20 minutes of adding the bromine. However, it was necessary to continue with the projected reaction scheme (10), if only to ascertain the nature of the optically-active "by-product".



Optically-active

(cont.)

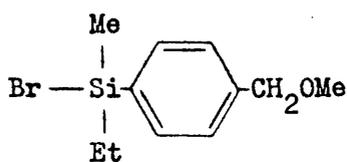


Because of the possibility of lithium aluminium hydride's reacting with carbon tetrachloride, the latter was removed at reduced pressure and replaced by diethyl ether in two experiments (p. 62). Since it is possible that racemisation of the bromosilane XX would be accelerated by its being concentrated in this way, in the third experiment the bromination and subsequent reduction were performed in pentane solution. Throughout, the temperature of the reaction mixture was kept below 35° when removing solvent. Despite these precautions, each of the three experiments yielded, on concentration, a solution having a rotation of ~ 0.1° -- very similar to that of the residue from reaction scheme 7, above (p. 93). Fractionation of the combined reaction mixtures removed a mixture of silanes (e.g., XXI), all optically-inactive, and left a residue (XXII) which was as optically-active as the unfractionated reaction mixture.

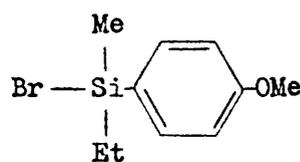
Fractionation of the silane mixture gave what seemed, from the refractive indices and infrared spectra, to be at least three different compounds, all containing the Si - H bond. Only one showed in its infrared spectrum the "ether band" at 1090 cm.⁻¹ (seemingly characteristic of the MeOCH₂- group since the band

is visible in the spectrum of the substituted benzyl methyl ether XIX only, not in any of its precursors), and its analysis (for carbon and hydrogen) was consistent with its being the required silane XXI (p. 98). The other two silanes are thought to be due to disproportionation of the required *p*-(ethylmethylsilyl)benzyl methyl ether (XXI), or, possibly, to bromine cleavage (reaction scheme 10, p. 98) of the α -methoxy-*p*-tolyl- instead of the *p*-methoxyphenyl-group from silicon (despite the great difference which would be expected in the reactivities of the Si - C bonds). The infrared spectra of the three silanes are given on p. 67, and the spectrum of the parent methyl ether XIX is given on p. 68.

As to the cause of the silane(s) thus produced being optically-inactive, it would seem that it is the bromine cleavage (reaction scheme 10) which is not stereospecific. However, this explanation is scarcely satisfactory since the bromination of the methyl ether XIX should be analogous to that of the methyl ester XIV, and the latter bromination appears at least partly stereospecific (p. 92). The reason might be that the two possible bromosilanes (XX and XXIII, below) are produced, and that they have opposite signs of rotation, thereby giving the observed appearance of non-stereospecificity.



XX



XXIII

Exact cancellation of the two rotations would be unlikely, but because of the very low rotations of arylethylmethylsilyl compounds, a relatively large difference in the rotations due to the two components (XX and XXIII) (dependent on both the quantity and the specific rotation of each component) might yet be no greater than 0.01° and therefore not be significant.

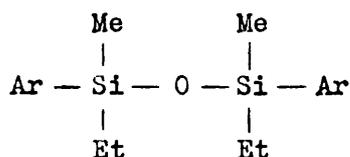
Now the p-methoxyphenyl - Si bond is cleaved by acid some 1500 times as fast as is the unsubstituted phenyl - Si bond.^{57b} No figure is available for the α-methoxy-p-tolyl - Si bond, but since the value for p-tolyl is 21 times that for phenyl, a reasonable estimate of the rate of acid cleavage of the α-methoxy-p-tolyl - Si bond is ~ 15 times that of the phenyl - Si bond. That is, the relative rates for acid cleavage of the p-methoxyphenyl - and the α-methoxy-p-tolyl - Si bonds should be ~ 100 : 1.

Other work in this Laboratory has shown⁵⁸ that competitive bromine cleavage of p-methoxyphenyl - and α-naphthyl - Si bonds leads to ~ 15 % cleavage of the latter (detected as α-bromonaphthalene), although the relative rates of acid cleavage for these two bonds are^{57b} 1500 : 8, i.e., ~ 200 : 1. In the present case, therefore, substantial bromine cleavage of the α-methoxy-p-tolyl - Si bond cannot be excluded.

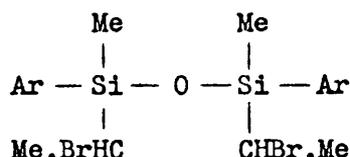
The residue (XXII) from reaction scheme 10 (p. 98), after three fractional distillations, afforded a substance (XXIV) which, although optically-active, was not pure on the evidence of its infrared spectrum. This spectrum, together with that of the parent

methyl ether XIX, and that of sym-di(p-carboxyphenyl)diethyldimethyl-disiloxane (p. 8), is given on p. 68. The residual Si - H and O - H bands (at 2100 cm^{-1} and 3300 cm^{-1} , respectively) were presumably due to small amounts of the lower-boiling components (of which these bands were characteristic) which were removed during the three distillations; the substance XXIV appeared to be mainly a disiloxane, from consideration of its infrared spectrum in the region 1000-1100 cm^{-1} , and had $[\alpha]_D^{20} + 0.89^\circ$ in benzene (c, 17.4).

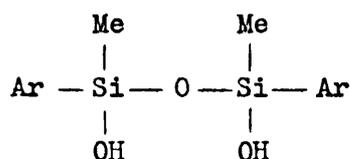
Halogen (i.e., bromine) was present in the substance XXIV, and the latter was therefore taken to be sym-diethyldimethyl-di(α -methoxy-p-tolyl)disiloxane (XXV) containing small quantities of compounds such as the related disiloxanes XXVI, XXVII, and XXVIII (and "mixed" products): $[\text{Ar} \equiv \text{C}_6\text{H}_4\text{CH}_2\text{OMe-p}]$



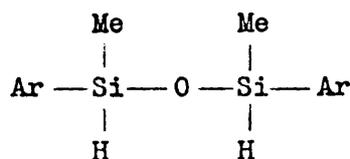
XXV



XXVI



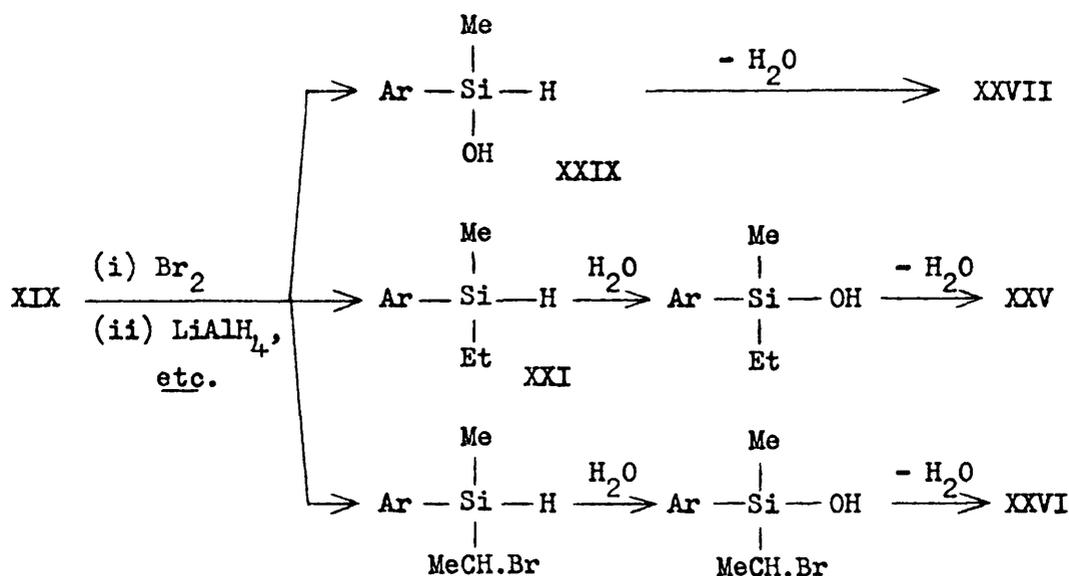
XXVII



XXVIII

It is suggested that this mixture was due to the following sequence of reactions: bromination of the substituted methyl ether XIX (p. 97) gave rise to the required bromosilane XX, and also small amounts

of both α -, and β -bromoethyl derivatives (with or without cleavage of an aryl - silicon bond in the same molecule). During the working up after the subsequent lithium aluminium hydride reduction, β -bromoethyl groups would be lost,^{57c} giving rise therefore to silanols (such as XXIX, below). In addition, hydrolysis of a proportion of the Si - H bonds gave silanols. Finally, these silanols eliminated water to produce disiloxanes, *i.e.*,



The optical-activity of the unknown substance XXIV might be due to one or several centres of asymmetry:

- (a) The two silicon atoms per molecule (assuming, as seems probable, the substance XXIV to be a disiloxane) might have retained their asymmetry so that the observed activity is due to the formation of a disiloxane that is not of the meso- form. The presence of Me.CH.Br- groups on some asymmetric silicon atoms, instead of Me.CH₂- groups, might explain the (for the present class of com-

pounds) rather high rotation observed.

- (b) The asymmetric carbon atom in the α -bromoethyl groups (assuming the bromine to be present in that form) might itself contribute to the observed optical rotation: the proximity of an asymmetric silicon atom at the bromination stage (reaction scheme 10, p. 97) could cause one configuration of the α -bromoethyl group to be formed in preference to the other, *i.e.*, a partial asymmetric synthesis might occur.^{59a} If the configuration of the silicon atoms was subsequently "lost", optical-activity would still be observed in the reaction mixture due to these α -carbon atoms.

In an attempt to determine whether the silicon atoms were the cause of the observed optical-activity, the unknown substance XXIV was dissolved in methanol and its rotation found to be $0.1^\circ \pm 0.005$. The solution was refluxed for 3 hours with concentrated aqueous hydrochloric acid solution (the maximum possible for homogeneity to be maintained), evaporated to dryness to remove all solvent, then redissolved in methanol to the same volume as before. The observed rotation was $0.09^\circ \pm 0.01$. Hence there was no practical change of rotation by this treatment. Had there been, it could have been concluded that the silicon atoms in substance XXIV were contributing to its optical-activity, since the methanol-hydrochloric acid treatment had brought into play the equilibrium between the disiloxane and the methoxysilane^{57d} (which would racemise under such conditions). The negative result obtained cannot

be used to deduce the opposite; the particular disiloxane under investigation might not be susceptible to acid-catalysed methanolysis. Accordingly, the reason(s) for the optical-activity of the unknown substance XXIV can only be surmised; it seems quite possible that the activity is due entirely to the α -carbon atoms (p. 103) in view of the optical instability, throughout these experiments, of the silicon atom in the arylethylmethylsilyl- system. Whether this apparent instability is merely due to the reactivity of the arylethylmethylsilyl- system allowing of rapid racemisation by a stereospecific but invertive mechanism, or to this system (by contrast with the methylphenyl(α -naphthyl)silyl- system) reacting by mixed invertive and retentive mechanisms, cannot be determined without its being possible to prepare an optically-active silicon-functional arylethylmethylsilyl- compound in order to test its optical stability -- in particular, to compare the rates of invertive and total exchange of the functional group. This last was the explicit aim of the work reported in this Thesis.

PART TWO: The Methanolysis of Optically-Active Tritium-Labelled

Methylphenyl(α -naphthyl)methoxysilane.

(A) The Preparation of the Substrates

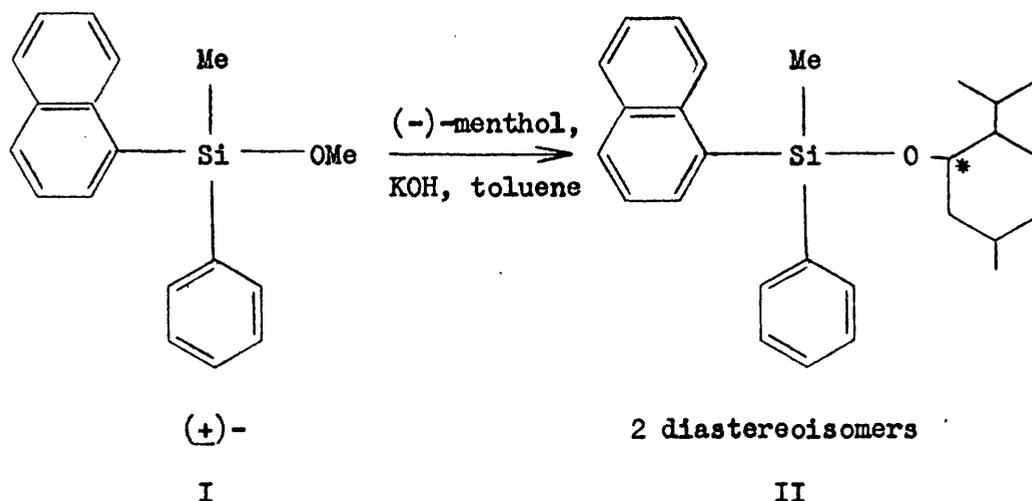
As noted above (p. 95) optically-active methylphenyl(α -naphthyl)methoxysilane was prepared, by the method²⁰ of Frye, during the course of the work presented in PART ONE of this Discussion, merely to check the technique

employed in the isopropoxysilane preparation described therein. When it became evident that the preparation of optically-active arylolethylmethylsilyl- compounds would be unsuccessful, it was decided to use methylphenyl(α -naphthyl)methoxysilane for the projected alcoholysis experiments, especially as there were (and are) no signs that Sommer intends to perform these experiments. In fact, the use of these methylphenyl(α -naphthyl)silyl- compounds for symmetrical-exchange investigations has the advantage that the results are more readily correlated with the known stereochemical behaviour of silicon(IV), since this system is the only one to have been studied to date (see p. 28).

The method employed for the preparation of the optically-active methoxysilane was as nearly as possible identical with that given by Frye;²⁰ the details are given in this Thesis only because they are not readily available elsewhere:-

Methylphenyldichlorosilane was converted to the corresponding dimethoxysilane using magnesium as the hydrogen chloride acceptor, following the general method of Fukakawa and Kohama.⁵⁵ Coupling of the dimethoxysilane with α -naphthylmagnesium bromide, following the instructions of Frye, gave racemic methylphenyl(α -naphthyl)-methoxysilane (I). The next step was the replacement of the methoxy group by the (-)-menthoxy group, and this was the only stage of the synthesis which gave trouble: despite refluxing the toluene solution for a total of 45 hours, there was obtained only a 36 % yield of the mixture of diastereoisomers II [Frye reported a 98 % yield,

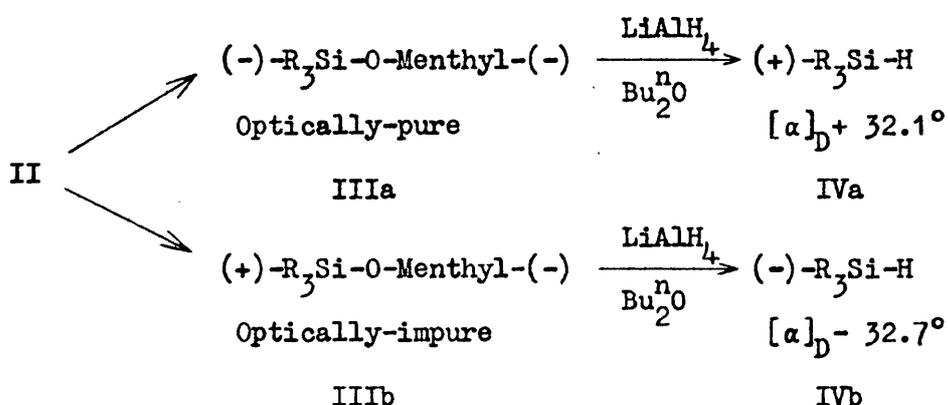
and refluxed the toluene solution for only 6 hours]:



The corresponding amount of unchanged methoxysilane and (-)-menthol was recovered. The reason for the low yield is not known, but it might be due to using somewhat impure racemic methoxysilane I as the starting material: using purified methoxysilane I, very high yields of the (-)-menthoxysilanes II were subsequently obtained in this Laboratory.⁵⁸

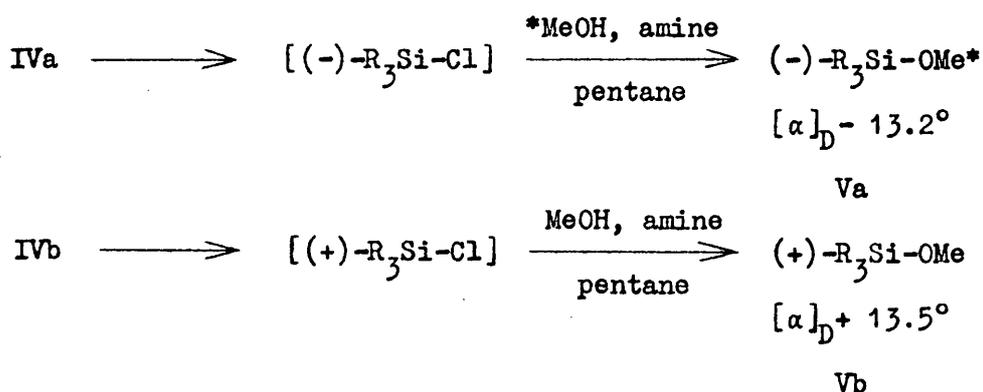
Separation of the two crystalline constituents (IIIa and IIIb) of the syrupy mixture of the diastereoisomers II was readily effected, but only one [the (-)-(-)- isomer, IIIa] was obtained optically-pure, since (as Frye points out²⁰) optical purity can be achieved at the next stage (*viz.*, the reduction by means of lithium aluminium hydride of the individual diastereoisomers III to the corresponding silanes IV): the phase properties of these silanes are such that excess (+)- or (-)-methylphenyl(α -naphthyl)silane can be separated by crystallisation from racemic silane. Accordingly, the mother liquors from the separation of the optically

pure (-)-menthoxide IIIa were reduced in toto, and the required (-)-silane IVb obtained from the product by subsequent crystallisation. Writing MePh(α -Np)Si as R_3Si throughout:



No attempt was made to obtain the silanes IV optically pure: their rotations indicated that the samples obtained were of the same optical purity as those employed by Frye for the interconversions outlined on p. 28, i.e., ~ 98 %.

Chlorination of the individual silanes IV, followed by immediate treatment with a pentane solution of anhydrous methanol (in one case labelled with tritium in the methyl group) and cyclohexylamine, again following Frye's method²⁰ in detail, gave the required optically-active methoxysilanes V:



It is of interest that trouble was experienced with continual separation of cyclohexylamine hydrochloride from the reaction mixture despite six thorough washings with water (Frye reports this difficulty also) since the same trouble was experienced in the analogous preparation of (p-carbamethoxyphenyl)ethylmethylisopropoxysilane (p. 95). The retention of the amine hydrochloride in the pentane solution was probably due to the presence of free amine in the solution, since crystallisation and separation of the impure optically active methoxysilanes V, followed by their dissolution in pentane and re-extraction with water, readily freed the methoxysilanes V from the amine hydrochloride. [Such a procedure was not of course possible for the compounds described in PART ONE of this Discussion.]

The specific rotation of each of the two optically-active methylphenyl(α -naphthyl)methoxysilanes thus prepared was rather lower than that reported by Frye: $[\alpha]_D +13.5^\circ$ (c, 4.60), and $[\alpha]_D -13.2^\circ$ (c, 4.99), as against Frye's value of $[\alpha]_D +16.5^\circ$ (c, 4.86), all in pentane solution.

(B) The Kinetics of Methanolysis of the Substrates

In view of Frye's statement that methylphenyl(α -naphthyl)methoxysilane is racemised "rapidly" in methanol (see p. 12), preliminary methanolyses were performed in a water-jacketted centre-filling polarimeter tube (with sealed-on end plates) as the reaction vessel. From these experiments, however, emerged two facts: the reaction rate was

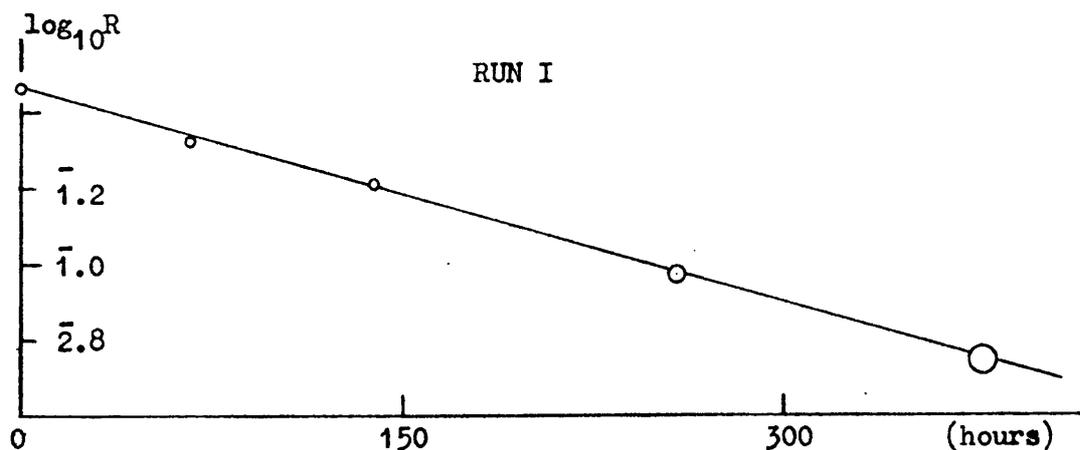
highly sensitive to traces of contaminant in the reaction vessel, and the uncatalysed ("neutral") reaction rate was extremely low. Owing to the nature of the polarimeter tube employed for these early experiments, drastic heat treatment had to be avoided, hence contamination could never be ruled out. Similarly, any observed difference in the rates measured polarimetrically and "radiochemically" (see below) using two separate solutions would not be reliable unless there was extensive repetition of experiments.

Accordingly, the method reported herein was evolved. The reaction mixture consisted of an approximately 1 % solution of the optically-active and tritium-labelled substrate in methanol at 24.97°, contained in a graduated flask (50 ml. or 100 ml.), catalyst being added as required. [To conserve substrate, not only was (-)-R₃SiOMe* employed, but also (+)-R₃SiOMe to which (-)-R₃SiOMe* was added to allow of radiochemical measurements being made.] At convenient intervals, solution (approximately 3 ml.) was removed, placed in an end-filling 2 dm. micro polarimeter-tube, and its rotation measured. Radiochemical measurements were performed by removing aliquots of the same reaction mixture and, after quenching the reaction, measuring the β-particle emission of the unreacted substrate as a galvanometer deflection.⁵⁶ These radiochemical measurements were performed by Dr. R. Baker and Mr. R. Spillett.

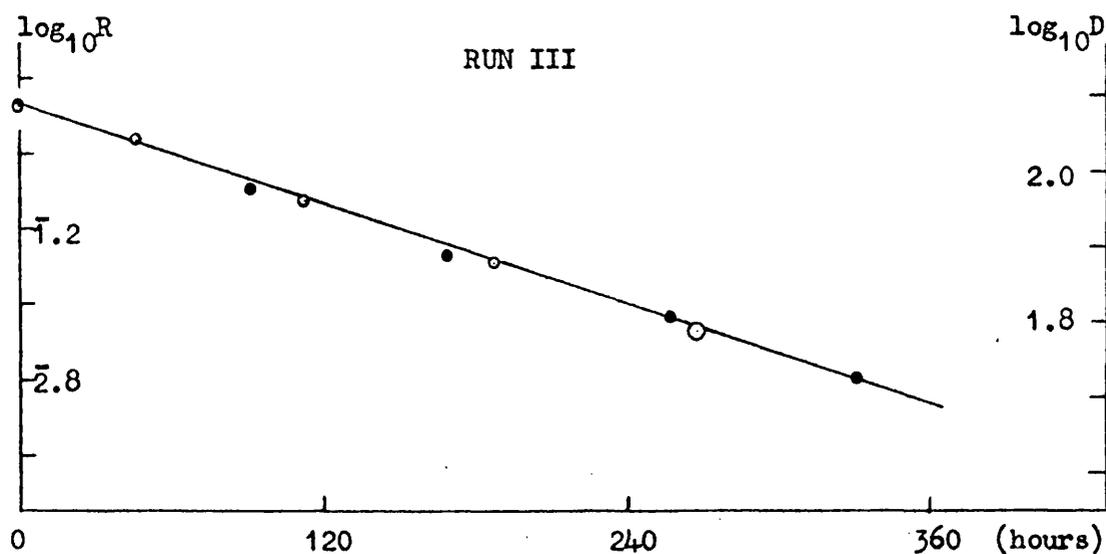
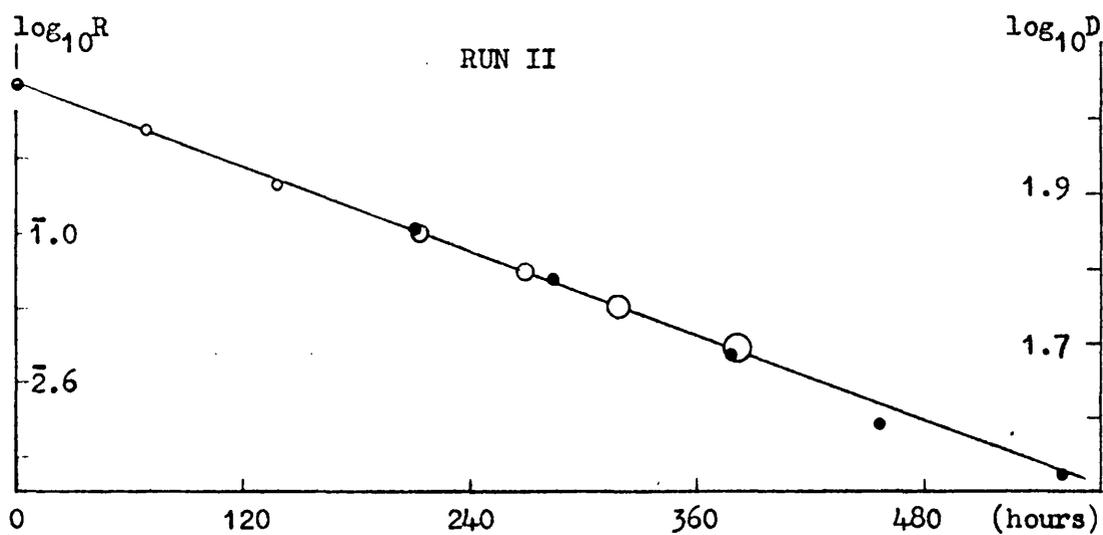
The results of these polarimetric and radiochemical measurements are discussed below; unless otherwise specified, a reaction rate refers to polarimetric measurements only.

(i) In neutral solution.

For the combined polarimetric and radiochemical measurements in neutral methanol, a mixture of (+)- R_3SiOMe and (-)- R_3SiOMe^* was used; the results (runs II and III) are presented here graphically. [In all the ensuing graphs, the size of the circle drawn round each polarimetrically determined point indicates (for rotations less than 0.2°) the effect of an error of $\pm 0.005^\circ$ in the polarimeter reading R . This value is considered to be the minimum instrumental error to be expected, since the smallest detectable imbalance of the polarimeter was 0.01° under optimum conditions. In addition to this source of error, it is possible that occasional anomalous readings were caused by the end-caps of the polarimeter tube being over-tightened. The filled-in circles drawn round the radiochemically-determined points of the accompanying graphs indicate the effect of an (arbitrary) error of $\pm 2\%$ in the net galvanometer deflections D ; the main source of error was probably in the pipetting of the 1 ml. or 2 ml. aliquots of reaction mixture.]



Run I (above) consisted of polarimetric measurements only, employing $(-)\text{-R}_2\text{SiOMe}^*$ without diluent; it is included here to show that the two isomers racemised at the same rate (within experimental error), and therefore that the two isomers were equally uncontaminated by a catalytic impurity such as cyclohexylamine hydrochloride, which persisted during their preparation (see p. 108).



N.B. The values for the rate constants obtained graphically and given in the Experimental section (p. 76) were obtained from individual graphs; the purpose of the graphs presented in this Discussion is to show that a single line suffices to describe both the polarimetric and the radiochemical measurements, and therefore the scales for $\log_{10} R$ and $\log_{10} D$ have been made to differ by a factor of 2 in order to compensate for the factor of 2 in the equation for k_{inv} (below). The origins of the $\log_{10} R$ scales have also been arbitrarily moved in these graphs to allow the polarimetrically- and radiochemically-determined lines to coincide.

The difference between the rates of runs II and III shows the effect of contamination, despite quite rigorous cleaning of the reaction vessels. However, it is clear from the graphs that within experimental error the rate of "invertive" exchange, specified by the pseudo first-order rate constant k_{inv} , is for a given run the same as the "total" rate of exchange, specified by the pseudo first-order rate constant k_{tot} , these rate constants being given by the following equations:

$$k_{inv} = \frac{2.303}{2t} \cdot \log_{10} \frac{R}{R_0} \quad (\text{ref. 59b}) \quad \dots\dots(1)$$

$$k_{tot} = \frac{2.303}{t} \cdot \log_{10} \frac{D}{D_0} \quad \dots\dots(2)$$

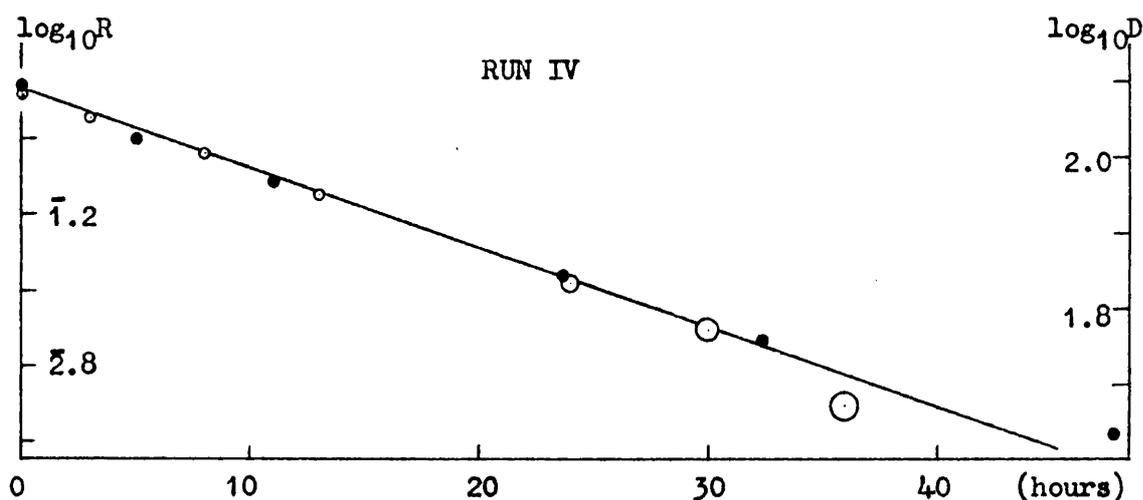
where R_0 and D_0 are respectively the observed rotation and the net galvanometer deflection at time = 0, and R and D are respectively the observed rotation and the net galvanometer deflection at

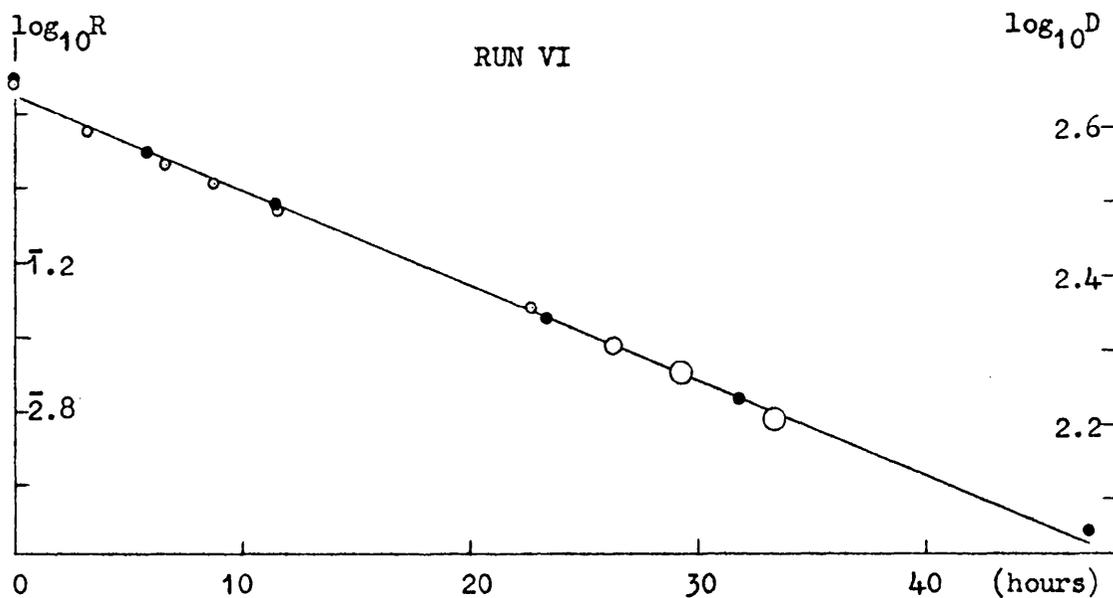
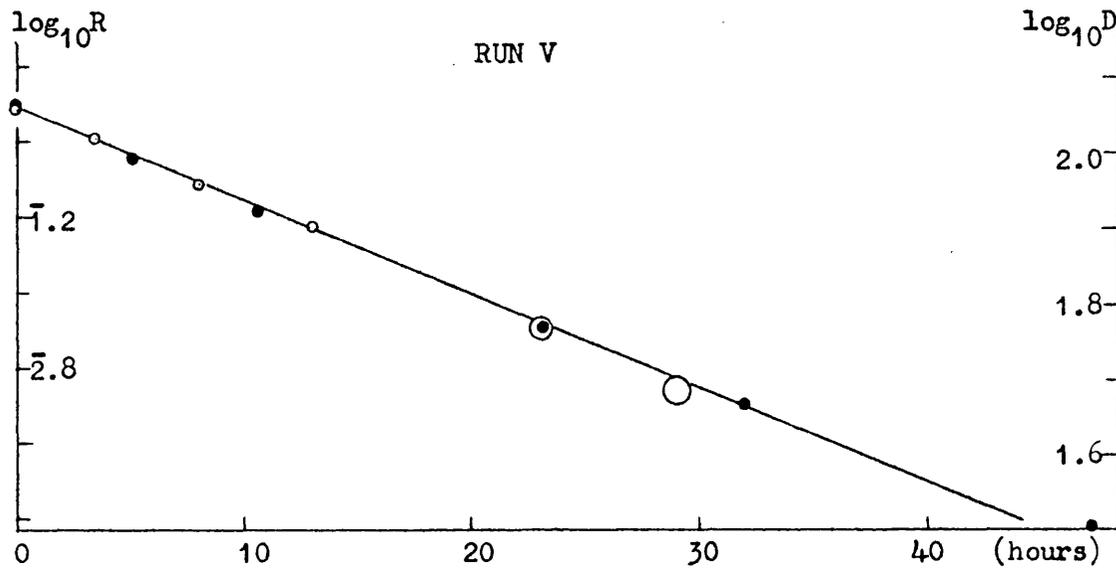
time = t.

The slow rate of methanolysis of methylphenyl(α -naphthyl)-methoxysilane in neutral methanol, although contrary to Frye's assertion, is not surprising since triphenylmethoxysilane (for example) is also known to react very slowly with neutral methanol. The comments on p. 26, concerning the significance of slow reaction rates of symmetrical substitution reactions at silicon, apply equally to the present case: despite the possible participation of d orbitals (with or without transition-complex formation) the activation energy for the reaction must be considerable.

(ii) In sodium acetate solution.

For runs IV, V, and VI, sodium acetate was added. Runs IV and V employed a mixture of (+)- R_3SiOMe and (-)- R_3SiOMe^* , but run VI employed undiluted (-)-isomer. For runs IV and V, the sodium acetate was added as a stock solution of nominal molarity 2.9×10^{-3} M, to give a reaction mixture which was nominally 1.45×10^{-3} M in sodium acetate.





Although straight lines were obtained (*i.e.*, the methanolysis was first-order in methoxysilane) the rates of runs IV and V were not consistent (but no less consistent than the rates obtained in neutral solution above) and further runs (not given) using the same catalyst stock solution proceeded at a rate too fast to meas-

ure - presumably because of contamination of the sodium acetate stock solution. Run VI, therefore, was performed by adding the catalyst as a solid to the reaction mixture, to give a solution which was nominally 1.13×10^{-3} M in sodium acetate, but in view of the small weight of catalyst involved this value could easily be in error by $\pm 5\%$.

The rate of run VI did not correspond well with the rates of runs IV and V, taking into account the nominal molarities of the reaction mixtures in catalyst; however, in each of these three runs the values of k_{inv} and k_{tot} were identical within experimental error.

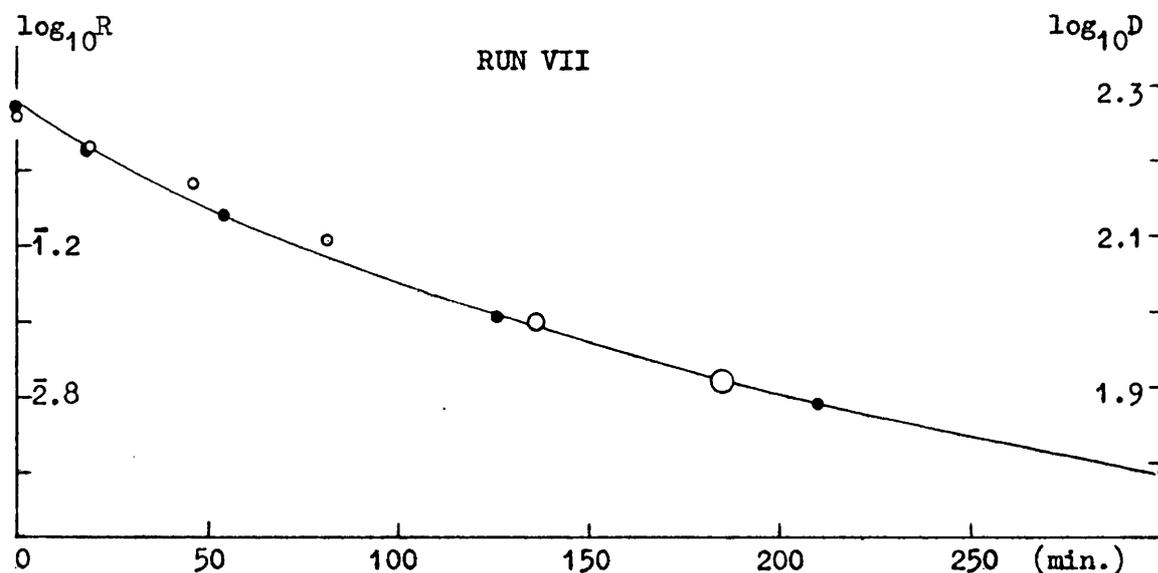
(iii) In sodium methoxide solution.

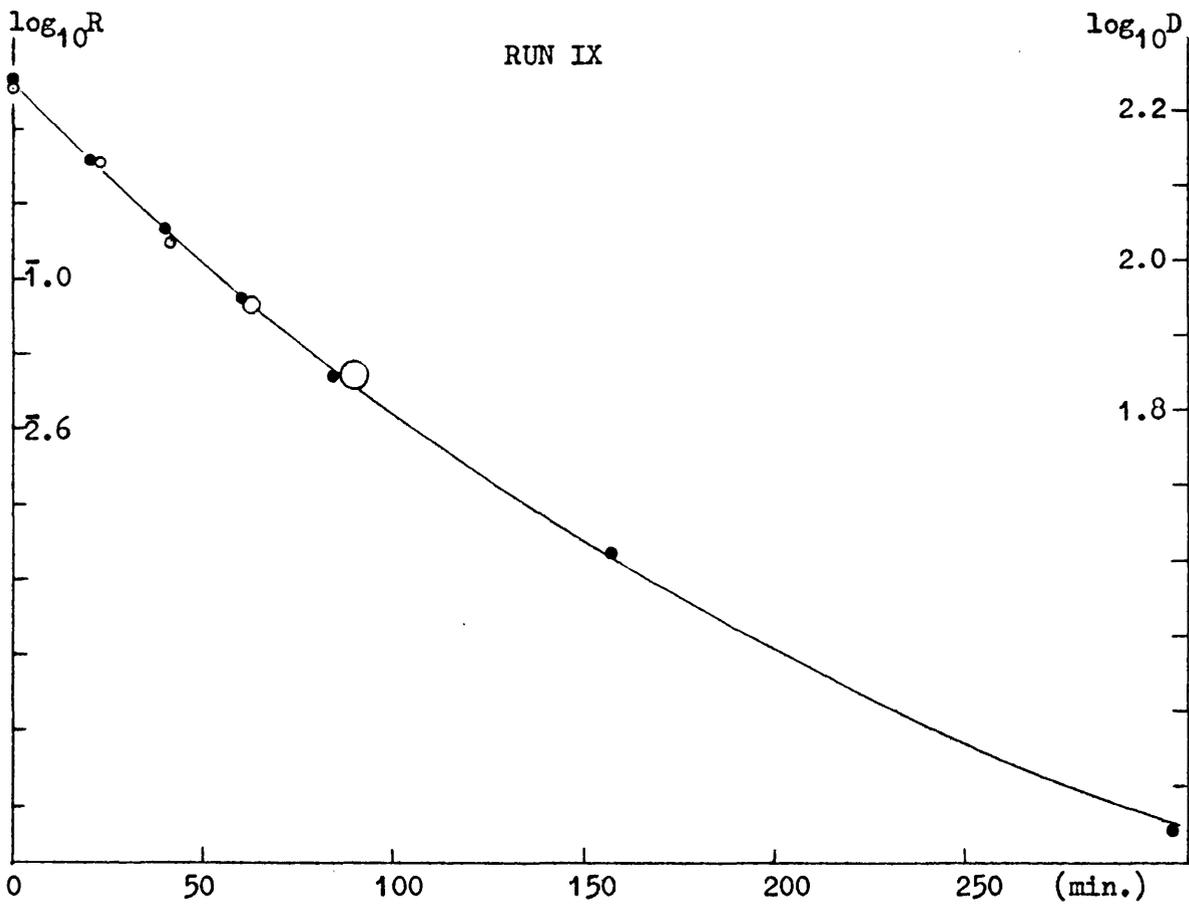
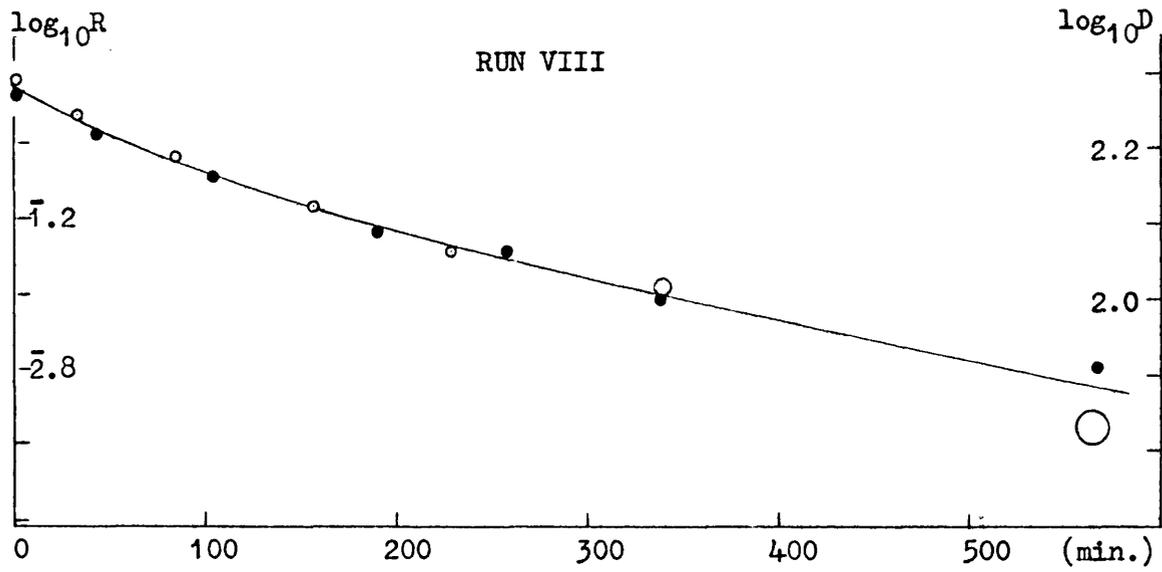
For runs VII, VIII, and IX, sodium methoxide was added to the reaction mixture as a 1.97×10^{-3} M stock solution, to give reaction mixtures that were nominally between 4×10^{-5} M and 6.2×10^{-5} M in sodium methoxide. In each run, undiluted $(-)-R_3SiOMe^*$ was employed.

By contrast with the previous runs (I to VI, inclusive), the observed rates were sufficiently large to warrant a correction due to the fact that some 5-10 minutes necessarily elapsed between withdrawal of a sample and measurement of its rotation. The times quoted for runs VII onwards ($k_{inv} > 100 \times 10^{-7} \text{ sec.}^{-1}$) are, therefore, the times at which rotations were measured, it being assumed that the rate of reaction in the polarimeter tube (at $\sim 20^\circ$) was substantially that at 25.0° . The effect of such an "over-correction",

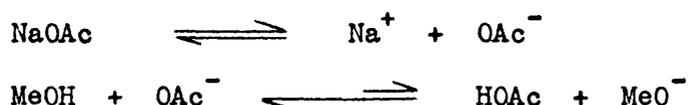
if observable, would be to give a value of k_{inv} less than its true value, i.e., to emphasise any difference between k_{inv} and k_{tot} . Since, within experimental error, $k_{inv} = k_{tot}$ for all of these runs, the above approximate correction is justified. [These corrections do not apply to the radiochemical measurements which allow of virtually instantaneous quenching of the reaction.]

Although an atmosphere of nitrogen was maintained in the reaction vessel during each of runs VII, VIII, and IX, the plots of $\log R$ vs. t , and of $\log D$ vs. t , were far from being straight lines for these runs; accordingly no graphical values for k_{inv} and k_{tot} are cited. Calculated values are given on p. 80. However, the two curves for each run were parallel, and showed the two rates (i.e., k_{inv} and k_{tot}) to be equal (within experimental uncertainty) at any given time.



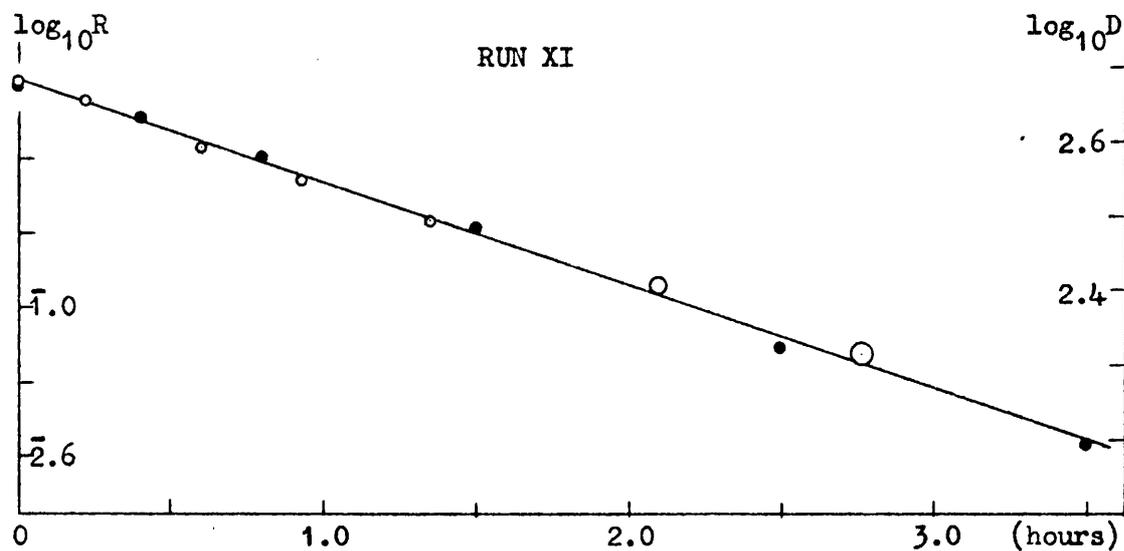
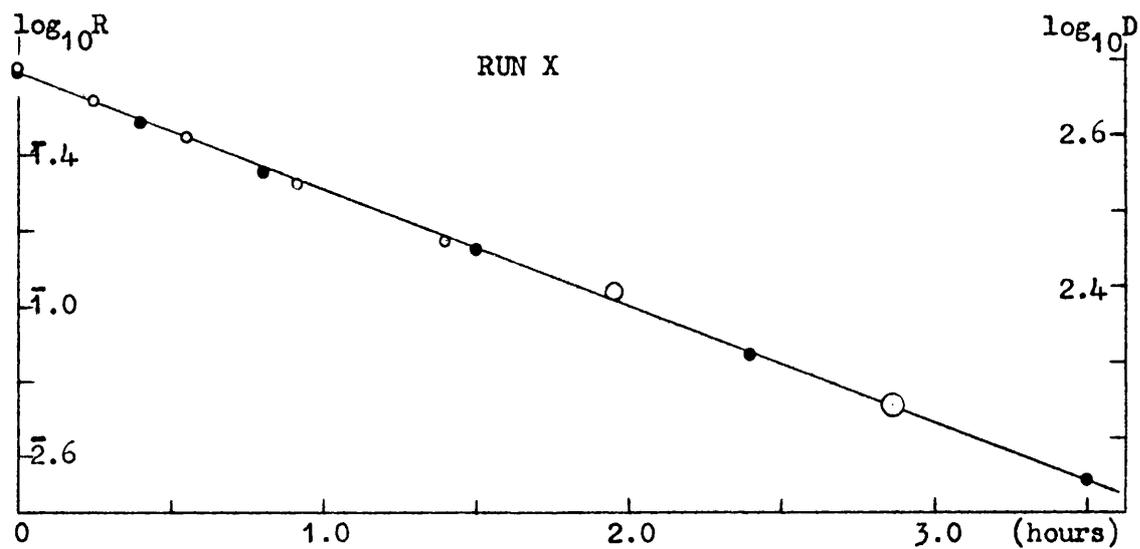


The reason for the curvature of these plots is not clear; it seems that despite the atmosphere of nitrogen, catalyst was "destroyed", either by the interaction of atmospheric carbon dioxide or water vapour, or by an acidic contaminant of the reaction vessel. No such difficulty was encountered when sodium acetate was used as the catalyst (without a nitrogen atmosphere), but the concentration of the acetate was rather higher than that of the methoxide (1×10^{-3} M as against 4×10^{-5} M), and furthermore sodium acetate is likely to have a buffering action since it gives rise to relatively little of the reactive species i.e., methoxide ions:



(iv) In benzoic acid solution.

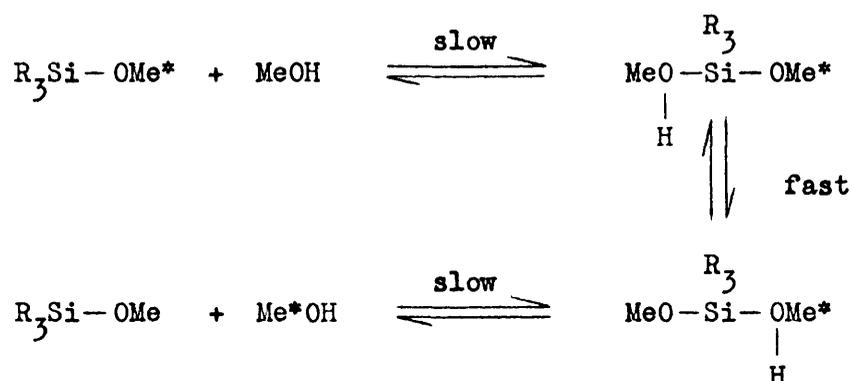
For runs X and XI, undiluted (-)- R_3SiOMe^* was employed, and the catalyst was added as a solid to the reaction mixtures to give solutions which were respectively 1.1×10^{-3} M and 0.95×10^{-3} M in benzoic acid. Straight lines were obtained from plots of $\log R$ vs. t , and $\log D$ vs. t , and the rates were consistent with the nominal concentrations of benzoic acid. The graphs of runs X and XI (p. 119) show that for each of the acid-catalysed runs (as for the "neutral" and base-catalysed runs) the rate of "invertive" exchange of the methoxyl group in methylphenyl(α -naphthyl)methoxysilane was identical with the rate of "total" exchange, within experimental uncertainty.



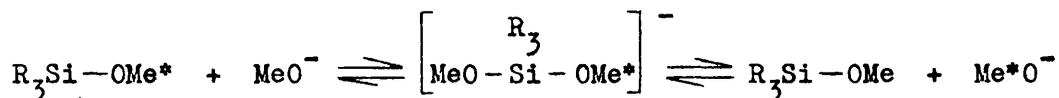
The mechanisms of the neutral, and acid and base catalysed, methanolyse described above are presumably as follows.³⁸ No assumptions are made as to the nature of the intermediates shown, or their stereochemistry.

Neutral solution. The reaction was first-order in the methoxy-

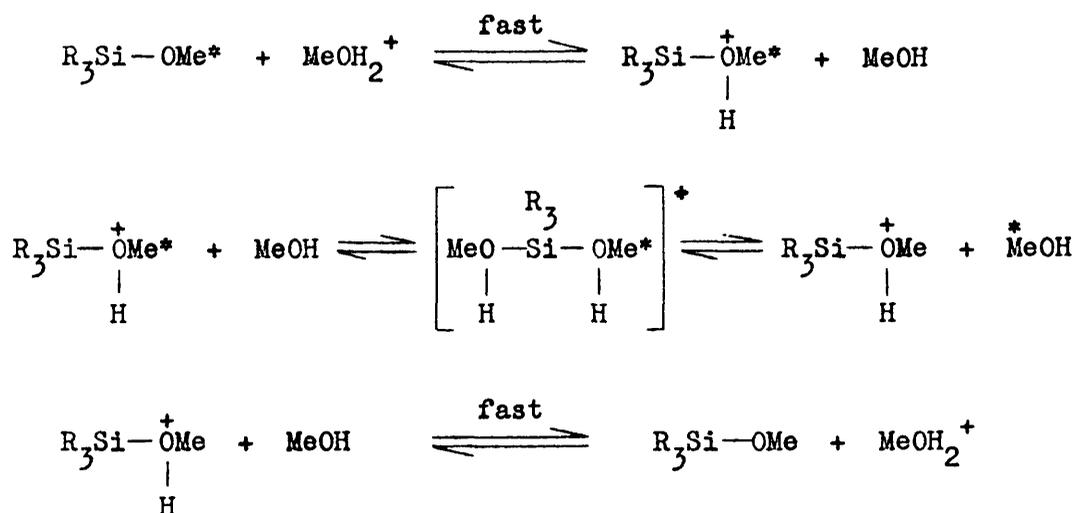
silane, and is consistent with the following equilibria:



Basic solution. The acetate-catalysed reaction was first-order in the methoxysilane, and it is possible (see p. 118) that the methoxide-catalysed reaction was also. The mechanism is probably:



Acidic solution. The benzoic acid-catalysed reaction was first-order in the methoxysilane. The mechanism is probably:



Clearly, methylphenyl(α -naphthyl)methoxysilane undergoes methanolysis with at least 95 % inversion of configuration, in neutral, acidic, and basic solution. To correlate this fact with the mechanisms which have been proposed for nucleophilic substitution at silicon, it is necessary to consider the stereochemical requirements of these mechanisms.

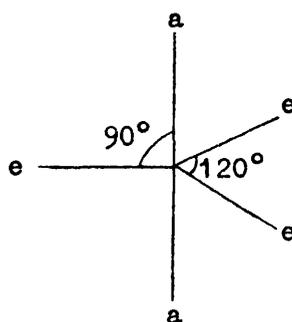
Now, the S_N2 -like mechanism unambiguously requires inversion of configuration, while the "expanded octet" mechanism can give rise to either inversion or retention of configuration: it seems to be accepted that, in the latter mechanism, "180°"-attack by the nucleophile leads to inversion (by analogy with the S_N2 -like mechanism), and that "90°"-attack by the nucleophile gives rise to retention of configuration. Only comparatively recently has the possibility of "120°"-attack been recognised, and the stereochemical consequences are not deemed predictable.³⁰ [The inverted commas serve to indicate that the angle cited is the final angle attained in the transition complex. During the formation of the complex the angle of attack of the nucleophile relative to the "leaving group" would probably be somewhat different.] Accordingly, an analysis is made here of the stereochemistry of the expanded octet mechanism.

PART THREE: The Stereochemical Consequences of the Expanded Octet Mechanism.

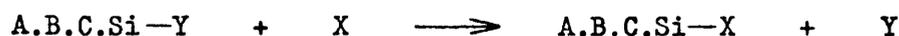
The following assumptions are made: a transition complex is

formed during the reaction; the transition complex is very similar to the transition states; the silicon atom in the complex is penta-covalent with sp^3d hybridisation; the geometry of the complex is that of a trigonal bipyramid.

The "groups" of such a transition complex can be distinguished according to whether they are situated "axially" or "equatorially" (a and e, respectively) thus:

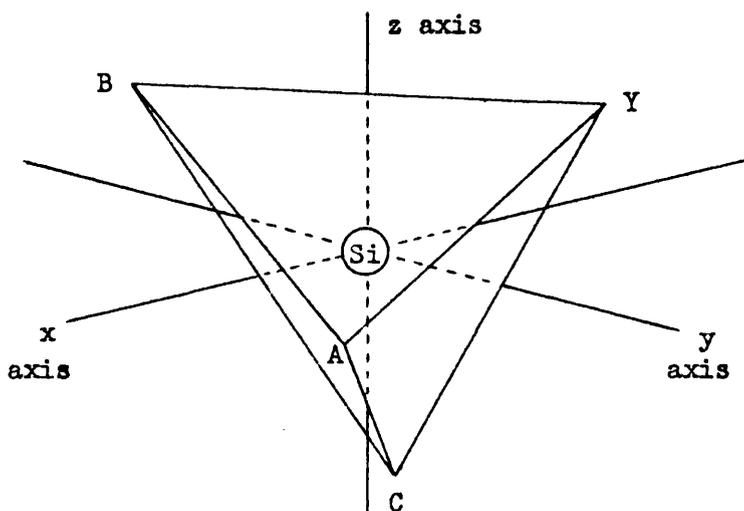


For convenience the three "inert" groups attached to the silicon atom throughout are designated A, B, and C. The leaving group is designated Y, and the entering group X, i.e., the reaction to be considered is



Since d orbital participation is fundamental to this mechanism, it is also necessary to consider the stereochemistry of the (empty) 3d orbitals of silicon. In the diagram (p. 123) is shown a regular tetrahedron, having the groups A, B, C, and Y at its apices, and a silicon atom at its centre. Also shown are the x, y, and z axes corresponding to the orientation of the silicon atom's p_x , p_y , and p_z orbitals which together with an s orbital constitute

the four sp^3 hybridised orbitals of the silicon atom. Now each of the six edges of the tetrahedron is a diagonal of one of the faces of a cube, the edges of which are parallel to the axes x , y , and z , and the centre of which coincides with their origin. Consequently, two $3d$ orbitals (the $d_{x^2-y^2}$ and the d_z^2) are directed out of the edges of the tetrahedron, e.g., in the plane defined by B, Si, and C.



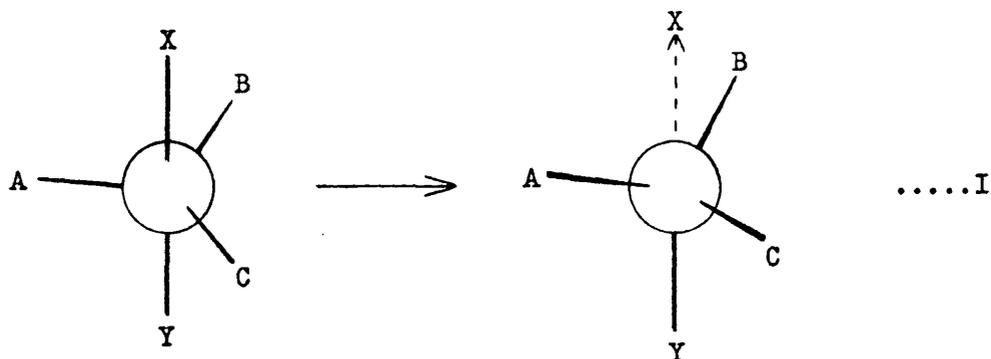
In between every pair of axes and at 45° to them there are the remaining three $3d$ orbitals (the d_{xy} , d_{yz} , and d_{xz}), which are therefore directed out of the "centre" of the faces of the tetrahedron, e.g., the face defined by B, A, and C.

The five $3d$ orbitals described above are no longer degenerate; the $d_{x^2-y^2}$ and d_z^2 orbitals are of equal energy, as are the d_{xy} , d_{yz} , and d_{xz} orbitals, but the former pair of orbitals are of lower energy than the latter three.

Considering again the transition complex, it follows from the "principle of microscopic reversibility" that formation of a

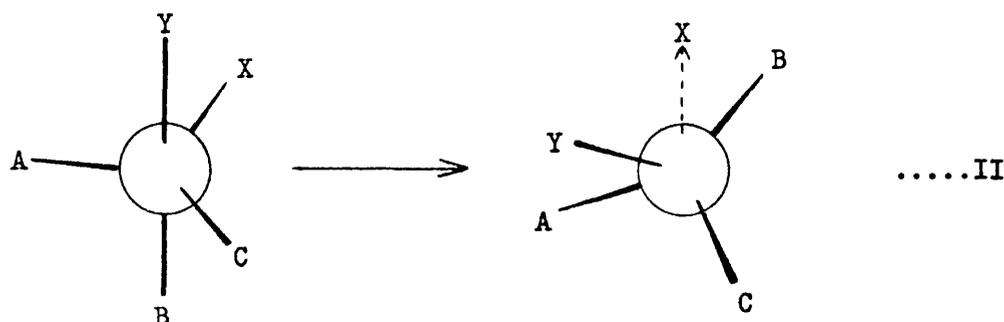
complex by the addition of a group X to a silicon(IV) compound A.B.C.Si-Y should be exactly reversed when X is eliminated, whatever might occur when the group Y is eliminated instead. If there is more than one way in which X can, seemingly, be eliminated, then there exists the same number of ways of forming the complex, and vice versa.

Given a transition complex in which all groups, though distinguishable, are sufficiently similar to avoid distortion of the trigonal-bipyramidal geometry, the elimination of either of the two axially-situated groups should follow the same stereochemical course (or choice of courses). Equally, the three equatorially-situated groups should be eliminated by a common steric course (or choice of courses) albeit different from that (or those) followed by the axial groups. Now, the elimination of an axial group (X, say) is formally similar to the breakdown of an S_N2 -like transition state, and it is reasonable to assume that no other stereochemical path is open to it:



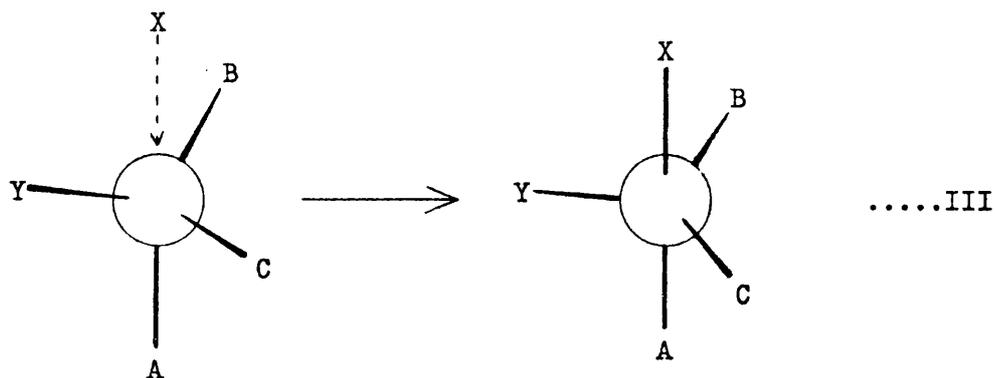
The elimination of an equatorial group (X, say) is less unambiguous, but one stereochemical course seems much more likely than the

others and so it is proposed that this course is the only one which in practice is available. [If this assumption is not accepted, no predictions as to the stereochemical consequences of "120°" and "90°" attack can be made.] This stereochemical course is as follows:



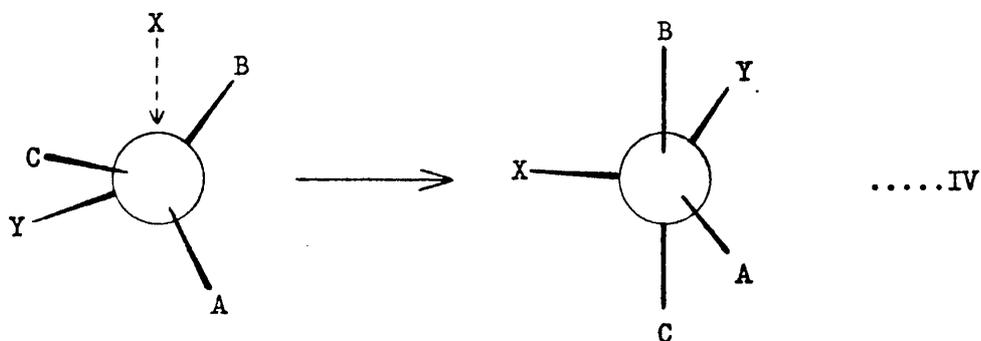
That is, the two axial groups, being the nearest ones to the leaving group X, "follow" X as it is eliminated, while the remaining groups, being equatorial and at 120° to each other, "close-up" to the tetrahedral angle of 109° 28'. In this fashion, the two pairs of groups A, C, and Y, B, maintain their mutual perpendicularity throughout the bond re-organisation. Any other stereochemical course would involve much more complicated bond movements.

Application of the principle of microscopic reversibility (p. 123) shows that formation of a complex may, therefore, only occur via the reverse of the two paths I and II. For example, when the entering group X is axial in the resultant complex, attack of X must have occurred (in the final stages, at least) at 180° to one of the groups A, B, C, or Y, which becomes the other axial group of the transition complex as follows:



Stereochemical path III is the reverse of path I (p. 124); the geometry is of course that of the S_N2 mechanism of substitution at carbon.

When the entering group X is to become equatorial in the resultant complex, this group X must attack in (for example) the plane B-Si-C, these two groups (B and C) becoming the axial groups of the transition complex:



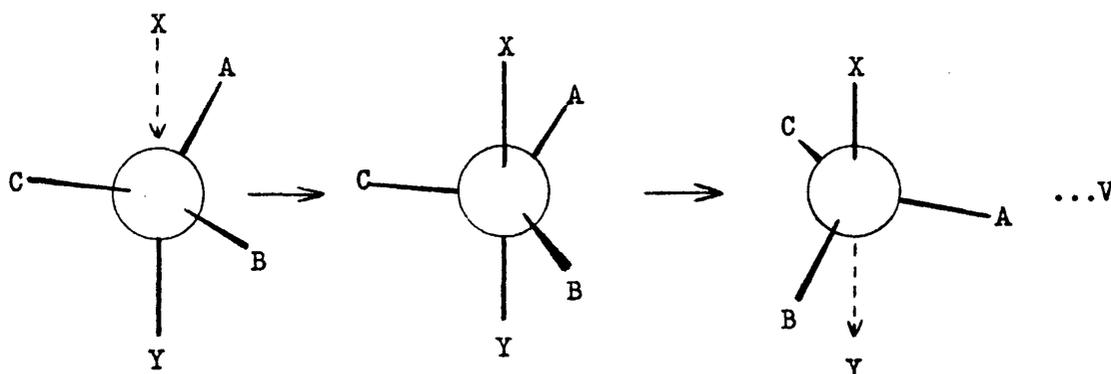
This path is the exact reverse of that given above (p. 125) for the elimination of an equatorial group (path II). Acceptance of the latter implies acceptance of the former.

Thus, stereochemical path III requires (in the limit) attack by a nucleophile at a tetrahedron face, while path IV requires (in the limit) attack by a nucleophile at a tetrahedron edge, and (as has been shown above, p. 123) these directions of attack correspond exactly with the orientation of the two varieties of d orbital available on a silicon atom.

On the basis of the stereochemical paths I and II (or III and IV) being exclusive, the stereochemical consequences of 180° , 120° , and 90° , attack at silicon are predictable:

180° attack.

By definition, 180° attack leads to a transition complex in which the two labile groups X and Y are both axial, and therefore formation and decomposition of the complex occurs via stereochemical paths III and I, respectively. E.g.:

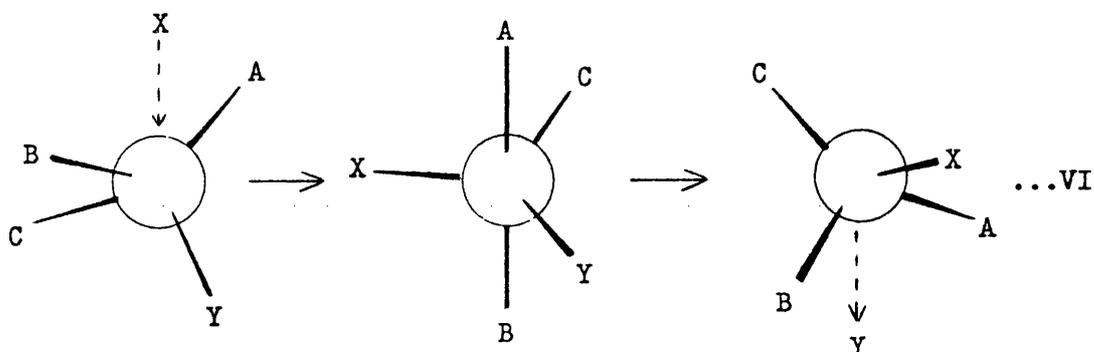


The stereochemical consequence is therefore INVERSION.

120° attack.

By definition, 120° attack leads to a transition

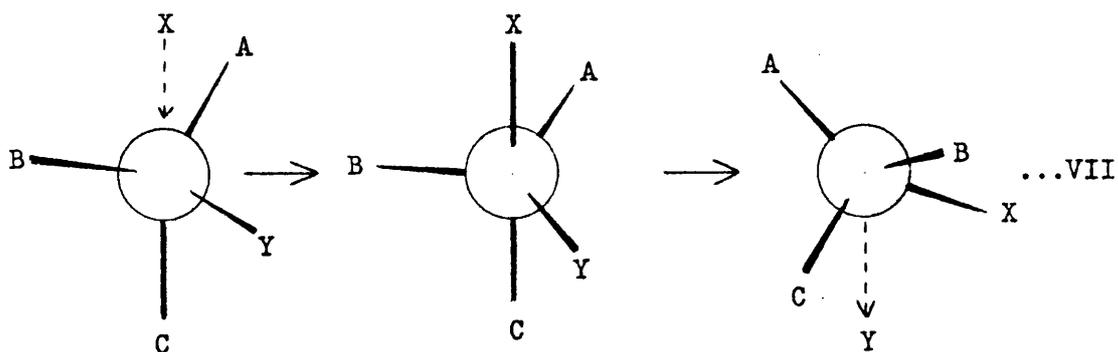
complex in which the two labile groups X and Y are both equatorial, and therefore formation and decomposition of the complex occurs via stereochemical paths IV and II, respectively. E.g.:

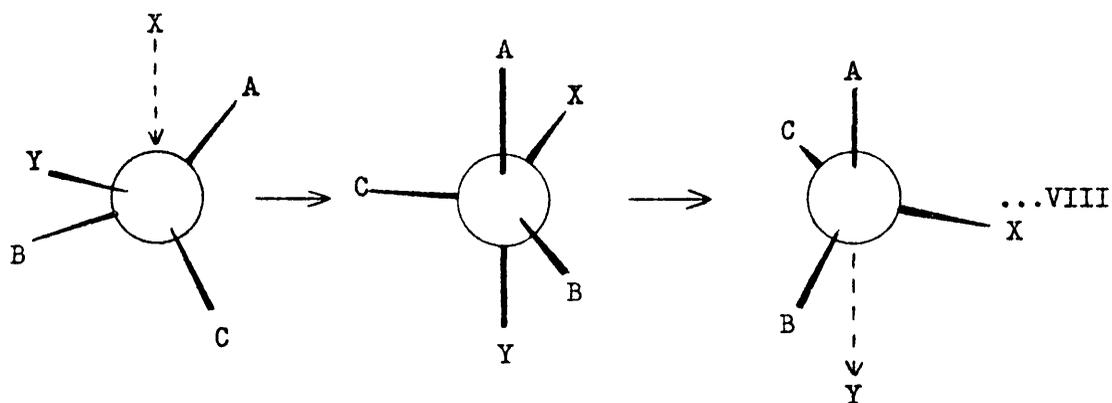


The stereochemical consequence is therefore INVERSION.

90° attack.

By definition, 90° attack leads to a transition complex in which one of the labile groups X and Y is axial and the other equatorial. Accordingly, either the complex is formed by the stereochemical path III then decomposed by path II (as in VII, below), or it is formed by path IV then decomposed by path I (as in VIII, below). E.g.:





The stereochemical consequence is therefore RETENTION, whichever of the two possible "90° complexes" is formed.

If A, B, C, X, and Y are identical, each attack at an edge of the tetrahedron involves the same potential energy barrier, which is different to the energy barrier common to attack at the tetrahedron's faces. On this picture, therefore, reaction via 180° attack involves two equal energy barriers, as does reaction via 120° attack; the relative magnitude of these barriers determines which of these two types of attack is predominant. On the other hand, reaction via 90° attack involves a potential energy barrier of the "180° type", and one of the "120° type", the sequence depending on which of the two possible "90° complexes" is formed. Thus for the special case of A, B, C, X, and Y being identical, reaction via 90° attack (irrespective of which complex is formed) should be at the same rate as reaction via the less-favoured of the other two modes of attack. Hence (if it were detectable) racemisation [90° + e.g.,

120° attack] plus inversion [in this case 180° attack] would be expected.

If A, B, C, and Y are different, but X = Y (as in the methanalysis of methylphenyl(α -naphthyl)methoxysilane described above, p. 108), then attack by X at each edge and at each face of the tetrahedron involves a different energy barrier to formation of the complex. 180° attack allows of no choice of the point of attack by the nucleophile, but the reaction profile is symmetrical when X = Y. 120° attack also gives rise to a symmetrical reaction profile when X = Y, but there are three reaction paths available since there are three suitably disposed edges to the tetrahedron. The reaction path is therefore determined by the lowest energy barrier associated with these three directions of attack.

"90° reaction" (paths VII and VIII, p. 128) can be initiated by attack at either of three faces, or at either of three edges, of the tetrahedron. In all six cases, the mode of elimination of Y (and therefore the energy barrier associated with it) is determined by the particular mode of attack: e.g., if the nucleophile X attacks at a particular edge AY (path VIII, p. 129), Y is eliminated from a particular face XCB. The reaction profile for each of the six possible reaction paths is unsymmetrical, the rate of each path being determined by the higher energy barrier. When X = Y, attack of the nucleophile X at an edge AY (say), followed by elimination of Y from the face XCB, is energetically identical to the attack of X at the face YCB followed by elimination of Y from the edge AX; the differ-

ence lies merely in the sequence of the energy barriers. Accordingly, when $X = Y$, there exist three pairs of reaction paths for 90° attack, each pair having a different rate-determining energy barrier. The preferred pair of reaction paths is the one whose rate determining energy barrier is the lowest of the three.

The observed identity of the rates of methanolysis of methylphenyl(α -naphthyl)methoxysilane measured polarimetrically and radiochemically (*i.e.*, the identity of k_{inv} and k_{tot} , pp. 108-121) implies, from consideration of the above stereochemical analysis, the actual or virtual absence of 90° attack in this reaction in all three systems studied, *viz* in acid, neutral, and basic solution. That is, the energy barrier to reaction via a " 90° complex" must be considerably higher (for this particular reaction) than the barrier to reaction via 180° or 120° (according to which of the latter modes of attack is the prevailing one). The reason for this disparity between the energy barriers of 90° attack and 180° (or 120°) attack is not clear from the above analysis; the latter assumes a model of the reaction path which shows that the three modes of attack can differ as to the energy barriers to be overcome, but not to the extent that 90° attack is completely eliminated (in practice). The only obvious factor in deciding at which edge or face of the tetrahedron attack leads to the easiest reaction path is the steric one. For example, the presence of the bulky α -naphthyl group together with the fairly bulky phenyl group on the silicon atom can conceivably cause 180° and 120° attack to be the preferred ones, simply because these modes

of attack lead to transition complexes in which α -naphthyl and phenyl groups are not at 90° to each other. However, in order that these two large groups may be axial in the complex, the nucleophile X must attack at that edge of the tetrahedron which is defined by these two large groups (i.e., 120° attack), while X must attack in the centre of the face bounded by all three "inert" groups if the two large groups are required in equatorial positions in the complex (i.e., 180° attack). It can therefore be argued that for the methylphenyl(α -naphthyl)silyl- system,

- (a) for steric reasons, the α -naphthyl and phenyl groups cause reaction via a " 90° complex" to be unfavourable compared with 120° or 180° attack;
- (b) for steric reasons, 180° attack is likely to be more favourable than 120° attack.

It is open to doubt that the steric factor is sufficient to explain the stereospecificity of those reactions of methylphenyl(α -naphthyl)-silyl- compounds which have been reported.

In all of the preceding, it has been assumed that full participation of a $3d$ orbital of silicon occurs in the transition complex to give five "equal" sp^3d hybridised orbitals for bond formation [the two axial bonds would be longer than the other three even in a perfectly "symmetrical" transition complex]. Sommer considers³⁰ this to be a limiting mechanism (an S_N2 -like mechanism being the other one) applicable only to "poor leaving groups" that require such activation as can be obtained by prior co-ordination

of the nucleophile to the silicon atom (p. 33). In considering the analogous participation of 3d orbitals in nucleophilic substitution at saturated carbon, Gillespie¹⁰ has proposed that the extensive reorganisation of hybridisation of the bonds to the "inert" groups constitutes a weakness of the mechanism, whereas the change from sp^3 to sp^2 hybridisation in the S_N2 mechanism causes if anything a strengthening of these bonds. Carrying this concept into silicon chemistry, it is plausible to argue that 180° attack by the expanded octet mechanism will be favoured (compared with other angles of attack by that mechanism) in any substitution at silicon in which it is possible, simply because it is formally similar (in geometry) to the "pure" S_N2 -like mechanism and need entail no more 3d orbital participation in the bonding to the "inert" groups than is necessary. Thus, instead of Sommer's concept of two limiting bimolecular mechanisms for nucleophilic substitution at silicon - a carbon-like S_N2 mechanism, and an expanded octet mechanism, the latter allowing of various angles of attack by the nucleophile - it seems reasonable to postulate that there are in effect three limiting bimolecular mechanisms. Two of these mechanisms are S_N2 -like mechanisms, one with full participation of a silicon 3d orbital, the other with no participation of a d orbital. The third mechanism is the " 90° -attack mechanism", necessarily involving full d orbital participation. If it is further postulated that the latter mechanism is (for the reasons given above) generally much less feasible energetically than the alternative S_N2 -like mechanism, but that under special (defined) con-

ditions it can be the more favoured mechanism, then it becomes possible to explain such stereochemical behaviour of silicon(IV) as has been reported.

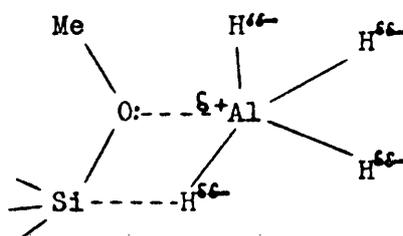
PART FOUR: An Explanation of the Observed Stereospecificity of
Nucleophilic Substitution at Silicon Situated in
Methylphenyl(α -naphthyl)silyl- Compounds.

One justification that Sommer gives for postulating the expanded octet mechanism³⁰ is that it is reasonable to assume the existence of a mechanism not available to carbon in order to explain the displacement from silicon of groups such as H and OMe, which are not (usually) displaceable from carbon. Now, silicon is more electro-positive than carbon [the electronegativities on the Pauling scale are 1.8 and 2.5, respectively⁵⁰], and this of itself is a valid reason for expecting groups that are displaceable from carbon by the S_N2 mechanism to be even more readily displaced likewise from silicon. Equally, it is to be expected on this basis that groups which are inert to nucleophilic displacement from carbon may yet be displaceable from silicon by an S_N2 -like mechanism. In addition, d orbital participation at some stage of the displacement is conceivable and indeed probable, thus it is reasonable in the light of the above arguments to assume that the "normal" mechanism of nucleophilic substitution at silicon is S_N2 -like - i.e., 180° attack of the nucleophile, together with the formation of possibly only one transition state. Nevertheless, the work of Sommer et al. on the reactivity of

bridgehead and related silanes and chlorosilanes (p. 19), and on the stereochemistry of nucleophilic displacements at silicon situated in the methylphenyl(α -naphthyl)silyl- system (p. 25), leaves no doubt that 90° attack of a nucleophile at silicon does occur. It is suggested here that 90° attack (necessarily involving extensive reorganisation of all the bonds during the reaction) is invoked only when the activation energy for the "normal" S_N2 -like reaction is prohibitive; either for steric reasons (as in bridgehead compounds), or because the leaving group and the nucleophile are both "poor" and there are special reasons for 90° attack being energetically more favourable than the alternative 180° (or 120°) attack.

The nature of the leaving group was the only constitutional factor considered by Sommer³⁰ (p. 32), but it is more logical to assume that the choice of mechanism may also be influenced by the nucleophilicity of the attacking species. That is, the energy obtained from bond making needs to be considered as well as the propensity of the leaving group - Si bond to heterolyse. Thus, very electronegative groups such as Cl are easily displaced by the S_N2 -like mechanism (*i.e.*, giving rise to inversion of configuration) even when the attacking nucleophile is poor (*e.g.*, " $LiAlH_4$ ", presumably AlH_4^-). A less electronegative group such as OMe is displaced by a sufficiently effective nucleophile (*e.g.*, OH^-) by the S_N2 -like mechanism; a much less effective nucleophile (*e.g.*, " $LiAlH_4$ ") displaces the OMe group by the S_N2 -like mechanism only very slowly, if at all. The observed retentive displacement of OMe by " $LiAlH_4$ " is here

postulated to be due to the formation of a cyclic transition state, which causes the displacement to be much more favourable energetically than it would be via a straightforward 90° attack:



The nucleophile in these reductions may not be the aluminohydride ion shown,²⁰ but nevertheless the principle remains the same: 90° attack under these circumstances is rendered energetically feasible because the nucleophilic attack at silicon is aided by electrophilic attack at the atom bonded to the silicon atom. On this hypothesis, the fact that no retention of configuration is detectable in the reduction of methylphenyl(α -naphthyl)chlorosilane by means of lithium aluminium hydride indicates that the S_N2 -like mechanism is potentially the preferred mechanism of nucleophilic substitution at silicon. It follows also that 90° attack will be detectable only under the following circumstances:

- (a) When the preferred S_N2 -like mechanism of a reaction involving a "good leaving group" and/or a "good entering group" is suppressed (as in bridgehead compounds). For example, the reduction and hydrolysis of bridgehead chlorosilanes (p. 19) involve a "good leaving group". [The fact that tri-*n*-butylchlorosilane is more reactive towards lithium aluminium hydride than is the almost

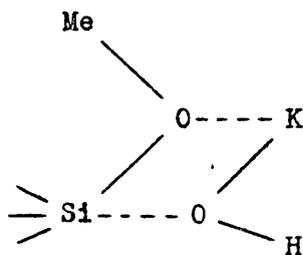
unstrained 1-chloro-1-silabicyclo[2.2.2.]octane (p. 24) also indicates that the S_N2 -like mechanism is the preferred one for chlorosilanes.] Alkaline hydrolysis of bridgehead silanes (p. 21) again involves a good nucleophile, even though the leaving group is poor.

- (b) When "normal" (*i.e.*, S_N2 -like) substitution at silicon is particularly unfavourable due to the nature of the leaving group and the nucleophile, but close proximity of these two "groups" in the transition state(s) facilitates the reaction in the manner outlined above.

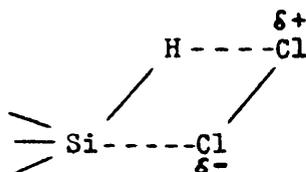
Of the reactions reported³⁰ by Sommer, the methylphenyl(α -naphthyl)silyl- system gave rise to 9 displacements in which configuration was thought to have been retained. These are listed below:

	Leaving Group	Attacking Reagent	Solvent	Entering Group	Stereochemical Path
1	OMe	KOH	xylene	OH	RETENTION
2	OMe	LiAlH ₄	Et ₂ O	H	"
3	OMe	Bu ^t MgCl	?	H	"
4	H	Cl ₂	CCl ₄	Cl	"
5	H	KOH	xylene	OH	"
6	D	LiAlH ₄	Et ₂ O	H	"
7	OSiR ₃	LiAlH ₄	Bu ⁿ ₂ O	H	"
8	OH	LiAlH ₄	Bu ⁿ ₂ O	H	"
9	OSiR ₃	KOH	xylene	OH	"

Sommer has suggested¹³ that the "retentive" cleavage of OMe from silicon by means of solid potassium hydroxide in xylene (reaction 1, p. 137) is due to the poorly ionising solvent favouring an "S_Ni-like" reaction of relatively undissociated complexes, as follows:

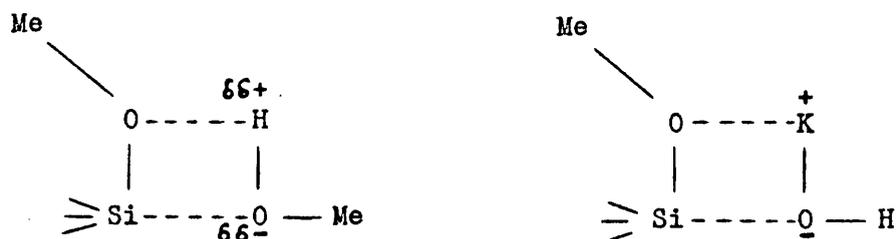


The remainder of the reactions listed on p. 137 are readily explained in the same way: reactions 5 and 9 are formally similar to reaction 1, and reactions 3, 6, 7, and 8 are all formally similar to reaction 2 (see p. 136). The chlorination of methylphenyl(α -naphthyl)silane by means of molecular chlorine (reaction 4) is also explicable in terms of a combined nucleophilic attack on the silicon and electrophilic attack on the hydrogen atom:



It is to be noted that in every case of retention reported, both the leaving group and the nucleophile are "poor", either inherently or because of the solvent employed. On the other hand, in the few reactions reported³⁰ wherein a "poor leaving group" was displaced

with inversion of configuration, the nucleophile was a "good" one. For example, the hydrolysis of methylphenyl(α -naphthyl)methoxysilane by aqueous hydroxide ion in acetone solution was found to be invertive. The fact that solid potassium hydroxide in xylene displaced Cl and MeC(=O) groups with inversion indicates again that an S_N2 -like mechanism is energetically preferable to an S_Ni -like mechanism when the leaving group is "good" enough. The uncatalysed methanolysis of methylphenyl(α -naphthyl)methoxysilane (p. 110) is a case of displacement of a poor leaving group by a poor nucleophile, and yet there is no sign of a "retentive" mechanism coming into play. On the above hypothesis, the inversion observed is due to an S_N2 -like displacement which is understandably slow because of the nature of the nucleophile and of the leaving group; an S_Ni -like mechanism is not likely because the hydroxyl hydrogen atom of a neutral methanol molecule cannot act as an electrophilic reagent as strongly as can the potassium atom of an "undissociated" potassium hydroxide molecule in the analogous hydrolysis reaction:



On this hypothesis, as on any other, there should exist a situation where the two mechanisms (S_N2 -like, and S_Ni -like) become

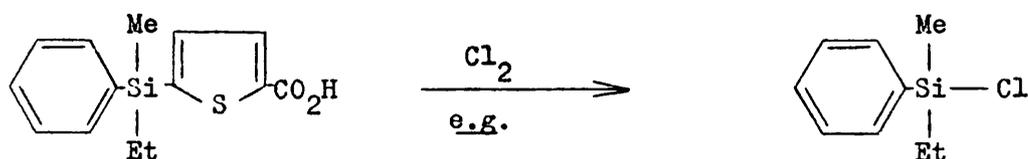
energetically comparable, giving rise to appreciable amounts of racemised product. Apparently this situation has never arisen in the methylphenyl(α -naphthyl)silyl system, and it is conceivable that a steric effect is in operation (cf. pp. 131-2) due to repulsions between the phenyl and α -naphthyl groups in the transition state(s), so that the energy difference between the S_N2 -like and S_N1 -like mechanisms is greater for this system than for the arylethylmethylsilyl system [described in PART ONE of this Discussion], thereby making the stereochemistry (i.e., the choice between the two mechanisms) much more clear cut. It is for this reason that the preparation and investigation of optically-active compounds other than those of the methylphenyl(α -naphthyl)silyl series is important.

PART FIVE: Future Investigations.

To test the generality of any deductions made on the basis of reactions involving the methylphenyl(α -naphthyl)silyl system, it is necessary to prepare an optically-active silicon-functional compound that is unlikely to have serious steric repulsions in the transition state(s) when undergoing nucleophilic substitution. Unfortunately, it is also necessary that the requisite silicon-functional compound (e.g., an alkoxide) should have a moderately large specific rotation if polarimetric measurements are to be made of its kinetics of racemisation. These two requirements are difficult to reconcile; had the preparation of optically-active arylethylmethylisopropoxysilane been successful (PART ONE of this Discussion) it

is doubtful whether it would have been usable for the projected alcoholysis investigations, since its specific rotation is probably much less than 1° . It is possible, however, that the use of an α -bromoethyl group instead of an ethyl group would increase the "asymmetry" of the silicon atom (*i.e.*, increase the specific rotation of the compound) without seriously affecting the steric repulsions between the "inert" groups during reaction.

As to the method of preparation of the requisite optically-active silicon-functional compound, it seems evident from PART ONE of this Discussion that resolution of a non silicon-functional compound followed by selective halogen cleavage of a single C - Si bond is unlikely to be satisfactory, if only because of the difficulty in removing the carbon-functional group whereby the resolution was effected. Pitt²⁹ has suggested the use of the 2-(5-carboxy)-thienyl group in the compound to be resolved since it is this group which should^{57b} be lost on treatment with halogen:



The alternative method, as employed by Sommer and Frye, is to resolve the required (*e.g.*) aryloethylmethylsilyl compound as a silicon-functional compound, using an optically-active (*i.e.*, asymmetric) functional group attached to the silicon atom. Whether or not this method of resolution is successful depends on the diastereoisomers being

solid, and on their being sufficiently different to allow of their separation. In the absence of groups such as CO_2H , asymmetric silicon compounds have a marked tendency not to be crystalline (PART ONE of this Discussion), requiring (as Frye²⁰ has pointed out) large groups such as α -naphthyl to impart crystallinity. Consequently this method may not in practice be usable for the preparation of optically-active organosilicon compounds in which no steric compression is likely in the transition state(s) during reaction.

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